(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 January 2003 (30.01.2003)

PCT

(10) International Publication Number
WO 03/007883 A2

(51) International Patent Classification[7]: A61K

(21) International Application Number: PCT/US02/22663

(22) International Filing Date: 16 July 2002 (16.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/906,963 16 July 2001 (16.07.2001) US

(71) Applicant *(for all designated States except US)*: **BRISTOL-MYERS SQUIBB PHARMA COMPANY** [US/US]; P. O. Box 4000, Route 206 and Provinceline Road, Princeton, NJ 08543-4000 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **NUGIEL, David** [US/US]; 8 Vanessan Court, Cherry Hill, NJ 08003 (US). **CARINI, David** [US/US]; 1921 Julian Road, Wilmington, DE 19803 (US). **DIMEO, Susan** [US/US]; 406 Clayton Avenue, Wilmington, DE 19809 (US). **VIDWANS, Anup** [IN/US]; 25 Angelica Drive, Avondale, PA 19311 (US). **YUE, Eddy** [US/US]; 9 Altemus Drive, Landenberg, PA 19350 (US).

(74) Agents: **PATEL, Rena** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543-4000 (US).

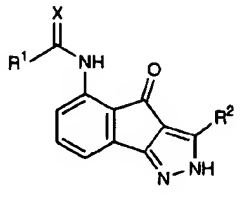
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ACYLSEMICARBAZIDES AS CYCLIN DEPENDENT KINASE INHIBITORS USEFUL AS ANTI-CANCER AND ANTI-PROLIFERATIVE AGENTS



(I)

(57) Abstract: The present invention relates to the synthesis of a new class of indeno[1,2-c]pyrazol-4-ones of formula (I) that are potent inhibitors of the class of enzymes known as cyclin dependent kinases, which relate to the catalytic subunits cdk1-7 and their regulatory subunits know as cyclins A-G. This invention also provides a novel method of treating cancer or other proliferative diseases by administering a therapeutically effective amount of one of these compounds or a pharmaceutically acceptable salt form thereof. Alternatively, one can treat cancer or other proliferative diseases by administering a therapeutically effective combination of one of the compounds of the present invention and one or more other known anti-cancer or anti-proliferative agents.

WO 03/007883 A2

TITLE

Acylsemicarbazides as Cyclin Dependent Kinase Inhibitors Useful as Anti-Cancer and Anti-Proliferative Agents

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part application of U.S. Serial No. 09/692,023, Filed October 19, 2000, entitled "ACYLSEMICARBAZIDES AND THEIR USES", which is a non-provisional filing of provisional application 60/160,713, filed October 20, 1999, entitled "ACYLSEMICARBAZIDES AS CYCLIN DEPENDENT KINASE INHIBITORS USEFUL AS ANTI-CANCER AND ANTI-PROLIFERATIVE AGENTS" which applications are herein incorporated by reference in their entirity as though set forth in full.

FIELD OF THE INVENTION

This invention relates generally to novel 5-substituted-indeno[1,2-c]pyrazol-4-ones which are useful as cyclin dependent kinase (cdk) inhibitors, pharmaceutical compositions comprising the same, methods for using the same for treating proliferative diseases, and intermediates and processes for making the same.

BACKGROUND OF THE INVENTION

One of the most important and fundamental processes in biology is the division of cells mediated by the cell cycle. This process ensures the controlled production of subsequent generations of cells with defined biological function. It is a highly regulated phenomenon and responds to a diverse set of cellular signals both within the cell and from external sources. A complex network of tumor promoting and suppressing gene products are key components of this

cellular signaling process. Over expression of the tumor promoting components or the subsequent loss of the tumor suppressing products will lead to unregulated cellular proliferation and the generation of tumors (Pardee, Science 246:603-608, 1989).

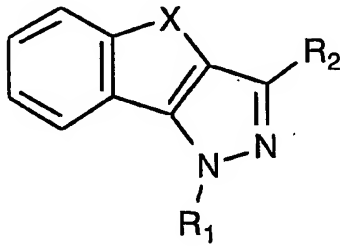
Cyclin dependent kinases (cdks) play a key role in regulating the cell cycle machinery. These complexes consist of two components: a catalytic subunit (the kinase) and a regulatory subunit (the cyclin). To date, six kinase subunits (cdk 1-7) have been identified along with several regulatory subunits (cyclins A-H). Each kinase associates with a specific regulatory partner and together make up the active catalytic moiety. Each transition of the cell cycle is regulated by a particular cdk complex: G1/S by cdk2/cyclin E, cdk4/cyclin D1 and cdk6/cyclinD2; S/G2 by cdk2/cyclin A and cdk1/cyclin A; G2/M by cdk1/B. The coordinated activity of these kinases guides the individual cells through the replication process and ensures the vitality of each subsequent generation (Sherr, Cell 73:1059-1065, 1993; Draetta, Trends Biochem. Sci. 15:378-382, 1990)

An increasing body of evidence has shown a link between tumor development and cdk related malfunctions. Over expression of the cyclin regulatory proteins and subsequent kinase hyperactivity have been linked to several types of cancers (Jiang, Proc. Natl. Acad. Sci. USA 90:9026-9030, 1993; Wang, Nature 343:555-557, 1990). More recently, endogenous, highly specific protein inhibitors of cdks were found to have a major affect on cellular proliferation (Kamb et al, Science 264:436-440, 1994; Beach, Nature 336:701-704, 1993). These inhibitors include $p16^{INK4}$ (an inhibitor of cdk4/D1), $p21^{CIP1}$ (a general cdk inhibitor), and $p27^{KIP1}$ (a specific cdk2/E inhibitor). A recent crystal structure of

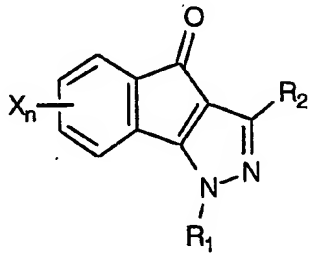
p27 bound to cdk2/A revealed how these proteins effectively inhibit the kinase activity through multiple interactions with the cdk complex (Pavletich, Nature 382:325-331, 1996). These proteins help to regulate the cell cycle through specific interactions with their corresponding cdk complexes. Cells deficient in these inhibitors are prone to unregulated growth and tumor formation.

This body of evidence has led to an intense search for small molecule inhibitors of the cdk family as an approach to cancer chemotherapy.

A series of indeno[1,2-c]pyrazoles having anticancer activity are described in JP 60130521 and JP 62099361 with the following generic structure:

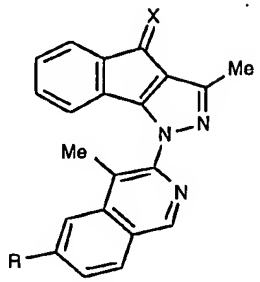


A series of indeno[1,2-c]pyrazoles having herbicidal activity are described in GB 2223946 with the following generic structure:



A series of 1-(6'-substituted-4'-methylquinol-2'-yl)-3-methylindeno[1,2-c]pyrazoles having CNS activity are

described by Quraishi, Farmaco 44:753-8, 1989 with the following generic structure:



There is a continuing unmet need for cdk inhibitors with which to treat proliferative diseases.

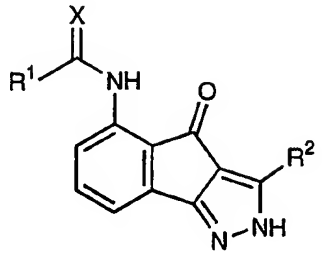
SUMMARY OF THE INVENTION

The present invention describes a novel class of indeno[1,2-c]pyrazol-4-ones or pharmaceutically acceptable salt forms thereof that are potent inhibitors of the class of enzymes known as cyclin dependent kinases, which relate to the catalytic subunits cdk 1-7 and their regulatory subunits know as cyclins A-H.

The present invention is also directed to a novel method of treating cancer or other proliferative diseases by administering a therapeutically effective amount of one of these compounds or a pharmaceutically acceptable salt form thereof.

A novel method of treating cancer or other proliferative diseases, which comprises administering a therapeutically effective combination of one of the compounds of the present invention and one or more other known anti-cancer or anti-proliferative agents is also described herein.

The present invention also describes compounds of formula (I):



(I)

wherein R_1, R_2 and X are defined below or pharmaceutically acceptable salts thereof as cyclin dependent kinase inhibitors.

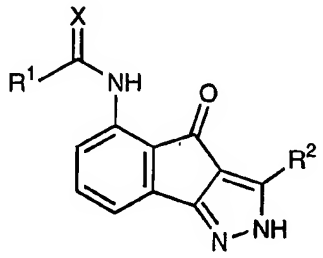
DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The invention pertains to novel cyclin dependent kinase inhibitors (cdks) and specifically, but not exclusively, as inhibitors of cdk/cyclin complexes. The inhibitors of this invention are indeno[1,2-c]pyrazol-4-one analogs. Certain analogs were selective for their activity against cdks and their cyclin bound complexes and were less active against other known serine/threonine kinases such as Protein Kinase A (PKA) and Protein Kinase C (PKC). In addition, these inhibitors were less active against tyrosine kinases such as c-Abl.

As described herein, the inhibitors of this invention are capable of inhibiting the cell-cycle machinery and consequently would be useful in modulating cell-cycle progression, which would ultimately control cell growth and differentiation. Such compounds would be useful for treating subjects having disorders associated with excessive cell

proliferation, such as the treatment of cancer, psoriasis, immunological disorders involving unwanted leukocyte proliferation, in the treatment of restinosis and other smooth muscle cell disorders, and the like.

The present invention, in a first embodiment, describes a novel compound of formula (I):



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

X is selected from the group: O, S, and NR;

R is selected from the group: H, C_{1-4} alkyl, and NR^5R^{5a};

R^1 is selected from the group: H, C_{1-10} alkyl substituted with 0-3 R^c, C_{2-10} alkenyl substituted with 0-3 R^c, C_{2-10} alkynyl substituted with 0-3 R^c, C_{1-10} alkoxy, -NHR^4, C_{3-10} carbocycle substituted with 0-5 R^a, and 3-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^2 is selected from the group: H, C_{1-10} alkyl substituted with 0-3 R^c, C_{2-10} alkenyl substituted with 0-3 R^c, C_{2-10} alkynyl substituted with 0-3 R^c, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^a, and 3-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, benzyl, C_{1-4} alkyl substituted with 1-3 R^c, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6; and

provided that if R^3 is phenyl, it is substituted with 1-5 R^a;

R^4 is independently at each occurrence selected from the group: H, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered

heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

provided that at least one R^3 is present and that this R^3 is selected from the group: C_{1-4} alkyl substituted with 1-3 R^6, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6;

R^a is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

alternatively, when two R^a's are present on adjacent carbon atoms they combine to form $-OCH_2O-$ or $-OCH_2CH_2O-$;

R^b is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3,

$CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, and SO_2R^{3b};

R^c is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^5NR^5R^{5a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

alternatively, R^3 and R^{3a}, together with the nitrogen atom to which they are attached, form a heterocycle having 4-8 atoms in the ring containing an additional 0-1 N, S, or O atom and substituted with 0-3 R^{3c};

R^{3b} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{3c} is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3b}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3b}$, $NHC(O)NR^3R^{3b}$, $NHC(S)NR^3R^{3b}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$,

$SO_2NR^3R^{3b}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

R^5 is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5a} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5b} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^6 is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^5R^5, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{3-10} carbocycle substituted with 0-5 R^5, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^5; and

m is selected from 0, 1, 2, and 3.

In another embodiment of the present invention, the compounds of formula (I) are selected from:

3-(4-methoxyphenyl)-5-(2-benzoylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-isonicotinoylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-nictinoylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(3,4-dihydroxybenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(4-hydroxybenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(3-aminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(4-aminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(2-aminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(4-N,N-dimethylaminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-phenethylacetylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

3-(4-methoxyphenyl)-5-(2-(2-hydroxybenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one; and

3-(4-methoxyphenyl)-5-(2-methoxycarbonyl hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

1-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-3-morpholin-4-yl-urea;

[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-urea;

1-(2-amino-cyclohexyl)-3-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-urea;

2-(4-aminomethyl-piperidin-1-yl)-N-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-acetamide;

1-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-3-morpholin-4-yl-urea.

or pharmaceutically acceptable salt form thereof.

Another embodiment of the present invention is a pharmaceutical composition comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula (I).

Another embodiment of the present invention is a method of treating cancer and proliferative diseases comprising: administering to a host in need of such treatment a therapeutically effective amount of a compound of formula (I), or a pharmaceutically effective salt form thereof.

DEFINITIONS

As used herein, the following terms and expressions have the indicated meanings. The compounds of the present invention may contain an asymmetrically substituted carbon atom, and may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomer form is specifically indicated.

The term "alkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, and s-pentyl. In addition, the term is intended to include both unsubstituted and substituted alkyl groups, the latter referring to alkyl moieties having one or more hydrogen substituents replaced by, but not limited to halogen, hydroxyl, carbonyl, alkoxy, ester, ether, cyano, phosphoryl, amino, imino, amido, sulfhydryl, alkythio, thioester, sulfonyl, nitro, heterocyclo, aryl or heteroaryl. It will also be understood by those skilled in the art that the substituted moieties themselves can be substituted as well when appropriate.

The terms "halo" or "halogen" as used herein refer to fluoro, chloro, bromo and iodo. The term "aryl" is intended to mean an aromatic moiety containing the specified number of carbon atoms, such as, but not limited to phenyl, indanyl or naphthyl. The terms "cycloalkyl" and "bicycloalkyl" are intended to mean any stable ring system, which may be

saturated or partially unsaturated. Examples of such include, but are not limited to, cyclopropyl, cyclopentyl, cyclohexyl, norbornyl, bicyclo[2.2.2]nonane, adamantly, or tetrahydronaphthyl (tetralin).

As used herein, "carbocycle" or "carbocyclic residue" is intended to mean any stable 3- to 7-membered monocyclic or bicyclic or 7- to 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl,; [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane (decalin), [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, or tetrahydronaphthyl (tetralin).

As used herein, the term "heterocycle" or "heterocyclic system" is intended to mean a stable 5- to 7- membered monocyclic or bicyclic or 7- to 10-membered bicyclic heterocyclic ring which is saturated partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and from 1 to 4 heteroatoms independently selected from the group consisting of N, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. If specifically noted, a nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the

heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1. As used herein, the term "aromatic heterocyclic system" is intended to mean a stable 5- to 7- membered monocyclic or bicyclic or 7- to 10-membered bicyclic heterocyclic aromatic ring which consists of carbon atoms and from 1 to 4 heterotams independently selected from the group consisting of N, O and S. It is preferred that the total number of S and O atoms in the aromatic heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H,6H-1,5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1,2,5-thiadiazinyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4aH-carbazolyl, b-carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2H,6H-1,5,2-dithiazinyl, dihydrofuro[2,3-b]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl., oxazolyl, oxazolidinylperimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, pteridinyl, purinyl, pyranyl, pyrazinyl,

pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6H-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, xanthenyl. Preferred heterocycles include, but are not limited to, pyridinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, indolyl, benzimidazolyl, 1H-indazolyl, oxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, or isatinoyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic,

succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 18th ed., Mack Publishing Company, Easton, PA, 1990, p. 1445, the disclosure of which is hereby incorporated by reference.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication commensurate with a reasonable benefit/risk ratio.

"Prodrugs", as the term is used herein, are intended to include any covalently bonded carriers which release an active parent drug of the present invention in vivo when such prodrug is administered to a mammalian subject. Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (i.e., solubility,

bioavailability, manufacturing, etc.) the compounds of the present invention may be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same, and compositions containing the same. Prodrugs of the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or in vivo, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug of the present invention is administered to a mammalian subject, it cleaves to form a free hydroxyl, free amino, or free sulfydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate, and benzoate derivatives of alcohol and amine functional groups in the compounds of the present invention.

"Substituted" is intended to indicate that one or more hydrogens on the atom indicated in the expression using "substituted" is replaced with a selection from the indicated group(s), provided that the indicated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O) group, then 2 hydrogens on the atom are replaced.

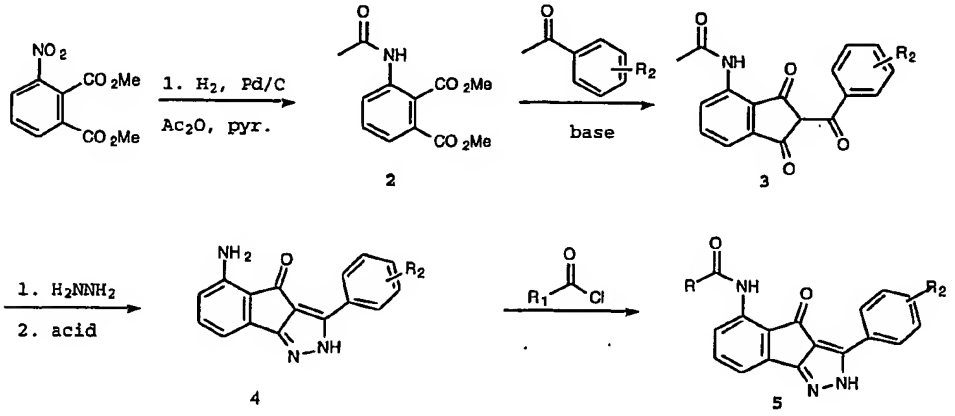
As used herein, the term "anti cancer" or "anti-proliferative" agent includes, but is not limited to, altretamine, busulfan, chlorambucil, cyclophosphamide, ifosfamide, mechlorethamine, melphalan, thiotepa, cladribine, fluorouracil, floxuridine, gemcitabine, thioguanine, pentostatin, methotrexate, 6-mercaptopurine, cytarabine, carmustine, lomustine, streptozotocin, carboplatin, cisplatin, oxaliplatin, iproplatin,

tetraplatin, lobaplatin, JM216, JM335, fludarabine, aminoglutethimide, flutamide, goserelin, leuprolide, megestrol acetate, cyproterone acetate, tamoxifen, anastrozole, bicalutamide, dexamethasone, diethylstilbestrol, prednisone, bleomycin, dactinomycin, daunorubicin, doxirubicin, idarubicin, mitoxantrone, losoxantrone, mitomycin-c, plicamycin, paclitaxel, docetaxel, topotecan, irinotecan, 9-amino camptothecan, 9-nitro camptothecan, GS-211, etoposide, teniposide, vinblastine, vincristine, vinorelbine, procarbazine, asparaginase, pegaspargase, octreotide, estramustine, hydroxyurea.

SYNTHESIS

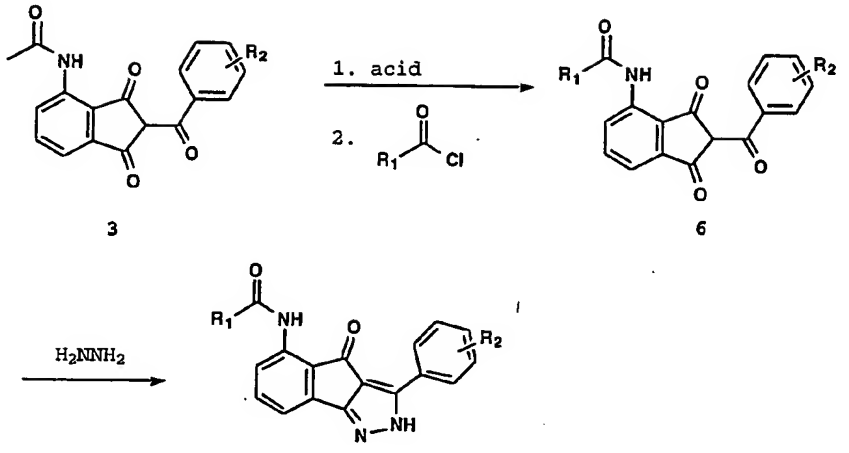
The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those methods described below. Each of the references cited below are hereby incorporated herein by reference.

SCHEME 1



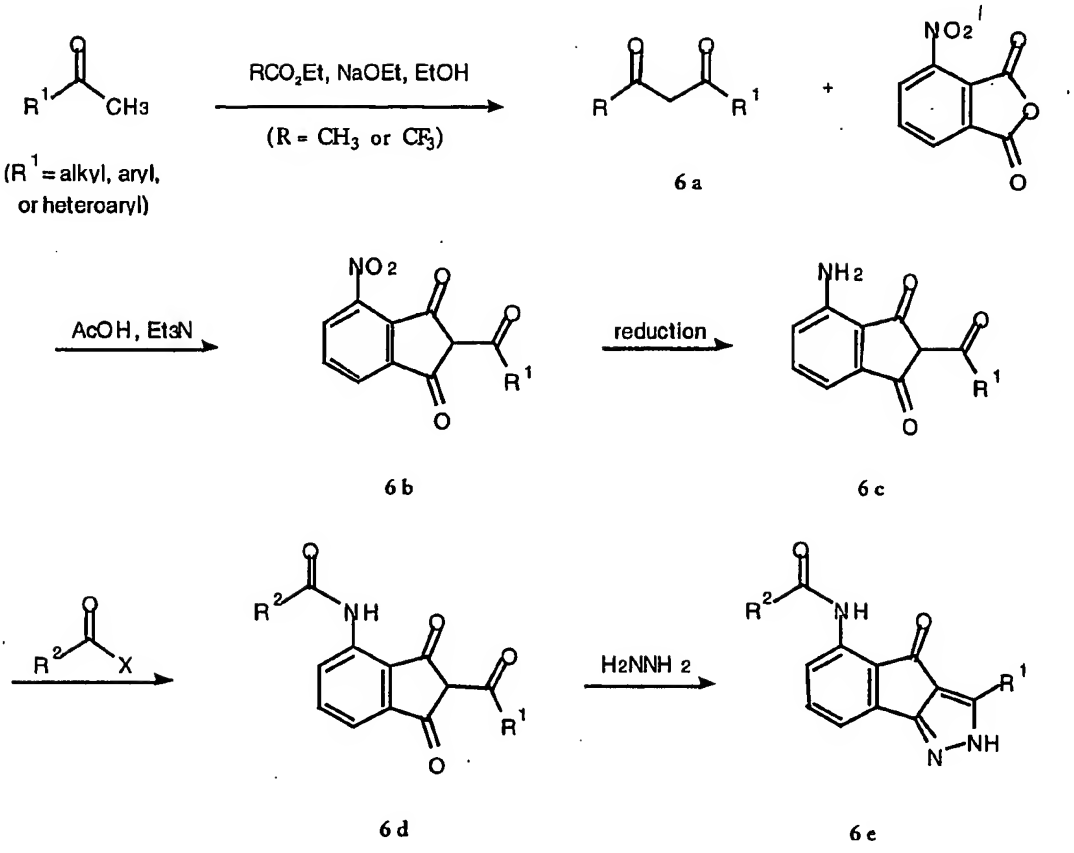
An approach to preparing indeno[1,2-c]pyrazol-4-ones is presented in Scheme 1 and can be used to prepare compounds of the present invention. The nitro group of dimethyl 3-nitrophthalate was reduced to the amine using catalytic hydrogenation. The aniline was acylated using acetic anhydride and pyridine as a base. A mixture of the resulting acetamide 2 and an acetophenone were treated with a strong base in an appropriate solvent at elevated temperature to give the desired triketone 3. Additional means of preparing triketones are known to one skilled in the art as described in Kilgore et al, Industrial and Engineering Chemistry 34:494-497, 1946, the contents of which are hereby incorporated herein by reference. The triketone was treated with hydrazine at elevated temperature in an appropriate solvent to give the indeno[1,2-c]pyrazol-4-one ring system. Additional means of preparing indeno[1,2-c]pyrazol-4-ones are known to one skilled in the art as described in Lemke et al., J. Heterocyclic Chem. 19:1335-1340, 1982; Mosher and Soeder, J. Heterocyclic Chem. 8:855-59, 1971; Hrnciar and Svanygova Collect. Czech. Chem. Commun. 59:2734-40, 1994 the contents of which are hereby incorporated herein by reference. The amide was deacylated by heating with a strong acid in an appropriate solvent to give aniline 4. This aniline was acylated under standard conditions using an acid chloride in an appropriate solvent to give the desired product 5.

SCHEME 2



An alternative method for making compounds of the present invention is shown in Scheme 2. The intermediate triketone 3 can be deacylated with strong acid and reacylated with an appropriate acid chloride using methods known to those skilled in the art. Subsequently, triketone 6 can the be converted to the indeno[1,2-c]pyrazol-4-one ring system using the same conditions described previously in Scheme 1.

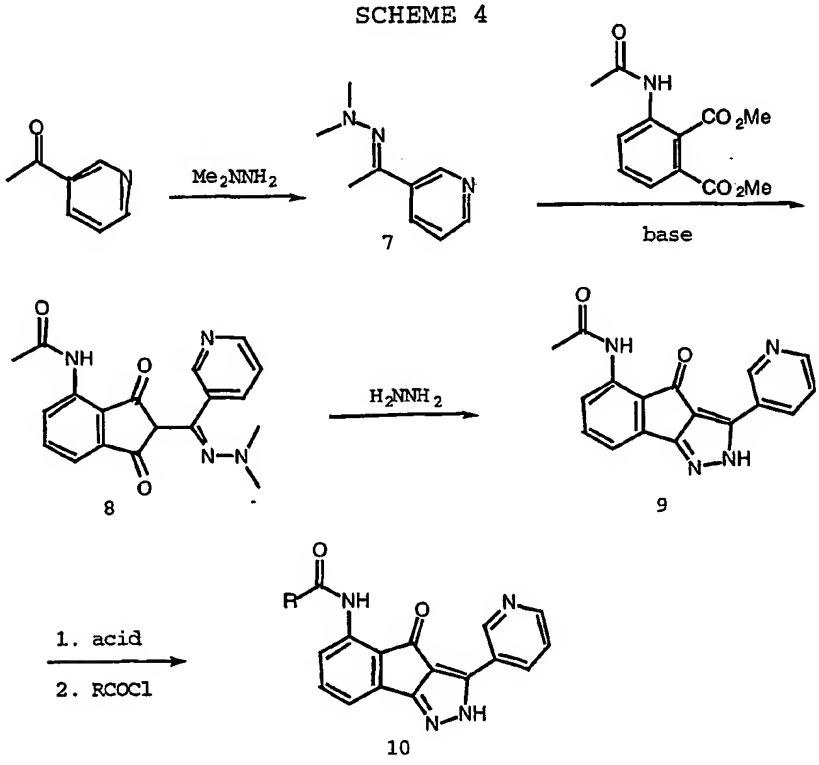
SCHEME 3



Another method for preparing the triketones 6 of Scheme 2 employs the condensation of a 1,3-diketone 6a with 3-nitrophthalic anhydride as described in Rotberg and Oshkaya, Zh. Organ. Khim. 8:84-87, 1972; Zh. Organ. Khim. 9:2548-2550, 1973, the contents of which are hereby incorporated herein by reference. The 1,3-diketones, when not commercially available can be readily prepared by one skilled in the art by the acetylation or trifluoroacetylation of the requisite methyl ketone, R^1COCH_3. Reduction of the nitro derivative 6b to the aniline 6c can be accomplished in a variety of ways including catalyic hydrogenation, treatment with zinc or iron under acidic conditions, or treatment with other reducing agents such as

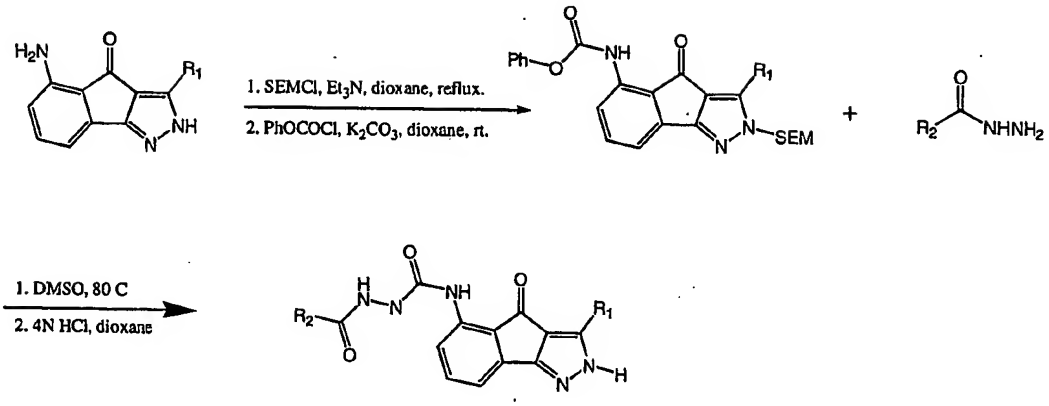
sodium dithionite or stannous chloride. Subsequently the aniline 6c can be converted to the indeno[1,2-c]pyrazol-4-ones of this invention by acylation followed by treatment with hydrazine as described previously in Scheme 2.

SCHEME 4



Another method for making the indeno[1,2-c]pyrazol-4-one ring system is shown in Scheme 4. Dimethyl hydrazine was reacted with 3-acetylpyridine with no solvent to give the hydrazone 7. This was treated in a similar fashion as described in Scheme 1 to give the desired intermediate 8. Additional means of preparing similar intermediates are known to one skilled in the art as described in Rappoport, J. Org. Chem. 49:2948-2953, 1984, the contents of which are hereby incorporated herein by reference. This intermediate was carried through the sequence in a similar fashion as described in Scheme 1.

SCHEME 5



Another approach to preparing indeno[1,2-c]pyrazol-4-ones is presented in Scheme 5 and can be used to prepare compounds of the present invention. Treating the intermediate 5-aminoindeno[1,2-c]pyrazol-4-one with 2-(trimethylsilyl) ethoxymethylmethyl chloride (SEMCl) and a suitable base in an inert solvent under reflux gives the SEM protected intermediate. The aniline is converted to the carbamate with phenylchloroformate using methods known to those skilled in the art. This intermediate is reacted with carbaztes in DMSO at elevated temperatures and then the SEM group is removed by treating with acid in a polar protic solvent to give the desired acylsemicarbazide-containing indenopyrazole analogs.

Other features of the invention will become apparent during the following descriptions of exemplary embodiments which are given for illustration of the invention and are not intended to be limiting thereof.

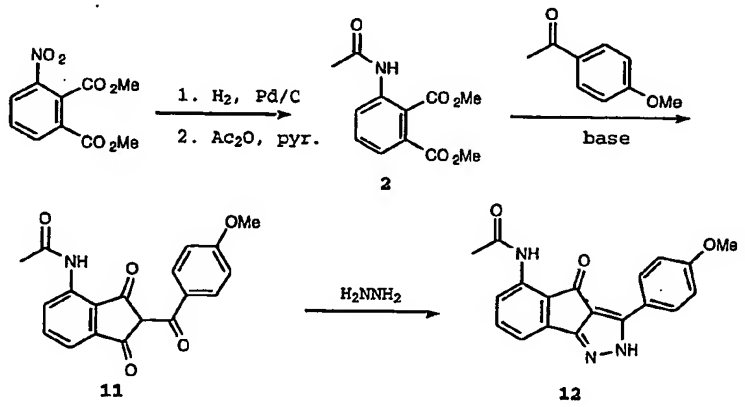
Examples

Abbreviations used in the Examples are defined as follows: "°C" for degrees Celsius, "CIMS" for chemical

ionization mass spectroscopy, "eq" for equivalent or equivalents, "g" for gram or grams, "h" for hour or hours, "mg" for milligram or milligrams, "mL" for milliliter or milliliters, "mmol" for millimolar, "M" for molar, "min" for minute or minutes, "p-TsOH" for para-toluenesulphonic acid, "DMF" for dimethylformamide, and "TFA" for trifluoroacetic acid.

Example I

Preparation of 3-(4-methoxyphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one



Step 1. Synthesis of 2 from dimethyl 3-nitrophthalate.

A solution of dimethyl 3-nitrophthalate (25 g, 105 mmol) in methanol (100 mL) was treated with 5% Pd/C (2.5 g) and hydrogenated on a Parr Shaker at 50 psi for 2 h. The solution was filtered (Celite), the filtrate collected and the solvent removed at reduced pressure. The residue was dissolved in acetic anhydride (20 mL) treated with pyridine (0.05mL) and heated to 80 °C for 1 min. The reaction was cooled and stirred at 25°C for 2 h. The solvent was removed at reduced pressure and the residue recrystallized from ethanol to give the product as a white solid (21 g, 79%). mp 104-105 °C; CIMS m/e calc'd for $C_{12}H_{14}NO_5$: 252.0872, found

252.0888; Analysis calc'd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58; found: C, 57.67; H, 5.29; N, 5.77.

Step 2. Synthesis of triketone 11 from 2.

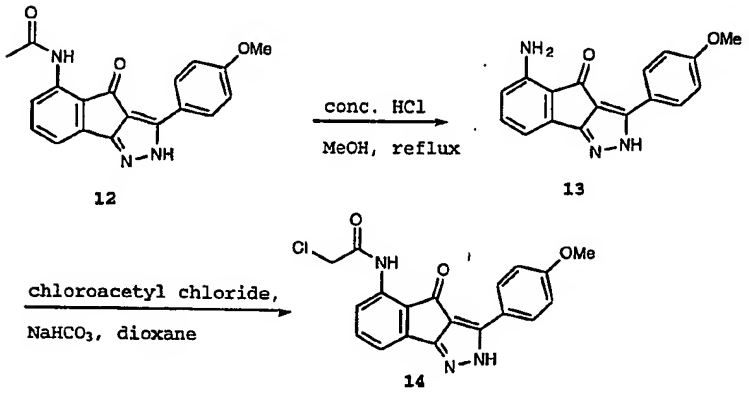
A solution of 2 (1 g, 4.0 mmol) in dry DMF (2 mL) was treated with sodium hydride (0.15 g, 60% suspension in oil, 0.4 mmol) in one portion. After 1 h, 4-methoxyacetophenone (0.6 g, 4.0 mmol) was added in one portion and the reaction heated to 90 °C. A second portion of sodium hydride (0.15 g, 60% suspension in oil, 0.4 mmol) was added and the exothermic reaction turns deep red. After 20 min, the reaction was cooled to 25 °C, diluted with water (20 mL), extracted with EtOAc (10 mL) and the aqueous phase separated. The aqueous phase was acidified with 2 N HCl to pH 2 and the crude product collected. Recrystalization with ethanol gave the desired product as a yellow solid (0.4 g, 30%). mp 174-175 °C; CIMS m/e calc'd for $C_{19}H_{16}NO_5$: 338.1028, found 338.1022; Analysis calc'd for $C_{19}H_{15}NO_5$: C, 67.65; H, 4.48; N, 4.15; found: C, 67.87; H, 4.29; N, 3.99.

Step 3. Synthesis of 12 from 11.

A solution of 11 (0.2 g, 0.6 mmol) in EtOH (5 mL) was treated with hydrazine hydrate (0.1 mL, 1.8 mmol) and p-TsOH (3 mg). The reaction was heated to reflux and stirred for 2 h. The reaction was cooled to 25 °C and the product collected as a yellow solid (0.1 g, 50%). mp 268 °C; CIMS m/e calc'd for $C_{19}H_{16}N_3O_3$: 334.1192, found: 334.1168; Analysis calc'd for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61; found: C, 68.81; H, 4.39; N, 12.45.

Example II

Preparation of 3-(4-methoxyphenyl)-5-(chloroacetamido)indeno[1,2-c]pyrazol-4-one



Step 1. Synthesis of 13 from 12.

A suspension of 12 (1.0 g, 3.0 mmol) in MeOH (10 mL) was treated with conc. HCl (1 mL) and heated to reflux. After 2 h, the reaction was cooled and the product was collected as a greenish solid (0.7 g, 81%). mp 273 °C; CIMS m/e calc'd for $C_{17}H_{14}N_3O_2$: 292.1086, found: 292.1080; Analysis calc'd for $C_{17}H_{13}N_3O_2$: C, 69.85; H, 4.83; N, 14.37; found: C, 69.99; H, 4.59; N, 14.44.

Step 2. Synthesis of 14 from 13.

A suspension of 13 (20 mg, 0.07 mmol) in dioxane (2 mL) was treated with aqueous sat. $NaHCO_3$ (1 mL) and chloroacetyl chloride (30 mL, 0.21 mmol). The reaction was heated to 50 °C and stirred for 2 h. The reaction was cooled, poured into water (2 mL), extracted with EtOAc (10 mL), the organic layer separated, dried ($MgSO_4$) and the solvent removed at reduced pressure. The solid residue was recrystallized from EtOH to give the product as a yellow solid (9 mg, 35%). mp 274 °C; CIMS m/e calc'd for $C_{19}H_{15}N_3O_3Cl$: 368.0802, found: 368.0818.

Example III

Preparation of 3-(4-methoxyphenyl)-5-(cyclopropylamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using cyclopropylacetyl chloride as the starting material. mp 289 °C; CIMS m/e calc'd for $C_{21}H_{18}N_3O_3$: 360.1348, found: 360.1330.

Example IV

Preparation of 3-(4-methoxyphenyl)-5-(isopropylamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using isopropylacetyl chloride as the starting material. mp 288 °C; CIMS m/e calc'd for $C_{21}H_{20}N_3O_3$: 362.1505, found: 362.1535.

Example V

Preparation of 3-(4-methoxyphenyl)-5-(ethylamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using propionyl chloride as the starting material. mp 287 °C; CIMS m/e calc'd for $C_{20}H_{18}N_3O_3$: 348.1348, found: 348.1313.

Example VI

Preparation of 3-(4-methoxyphenyl)-5-(cyclopentylamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using cyclopentylacetyl chloride as the starting material. mp 267 °C; CIMS m/e calc'd for $C_{23}H_{22}N_3O_3$: 388.1661, found: 388.1626.

Example VII

Preparation of 3-(4-methoxyphenyl)-5-(cyclobutylamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using cyclobutylacetyl chloride as the starting material. mp 297 °C; CIMS m/e calc'd for $C_{22}H_{20}N_3O_3$: 374.1505, found: 374.1530.

Example VIII

Preparation of 3-(4-methoxyphenyl)-5-(phenylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using phenylacetyl chloride as the starting material. mp 280 °C; CIMS m/e calc'd for $C_{25}H_{20}N_3O_3$: 410.1505, found: 410.1533.

Example IX

Preparation of 3-(4-methoxyphenyl)-5-(butylamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using butyryl chloride as the starting material. mp 282 °C; CIMS m/e calc'd for $C_{21}H_{20}N_3O_3$: 362.1505, found: 362.1500.

Example X

Preparation of 3-(4-methoxyphenyl)-5-((4-chlorophenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using 4-chlorophenylacetyl chloride as the starting material. mp 238 °C; CIMS m/e calc'd for $C_{25}H_{19}N_3O_3Cl$: 444.1115, found: 444.1110.

Example XI

Preparation of 3-(4-methoxyphenyl)-5-((3-methoxyphenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using 3-methoxyphenylacetyl chloride as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{26}H_{22}N_3O_4$: 440.1610, found: 440.1620.

Example XII

Preparation of 3-(4-methoxyphenyl)-5-((4-methoxyphenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using 4-methoxyphenylacetyl chloride as the starting material. mp 280 °C; CIMS m/e calc'd for $C_{26}H_{22}N_3O_4$: 440.1610, found: 440.1630.

Example XIII

Preparation of 3-(4-methoxyphenyl)-5-((3,4-dimethoxyphenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using 3,4-dimethoxyphenylacetyl chloride as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{27}H_{24}N_3O_5$: 470.1716, found: 470.1731.

Example XIV

Preparation of 3-(4-methoxyphenyl)-5-((2,5-dimethoxyphenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example II using 2,5-dimethoxyphenylacetyl chloride as the starting material. mp 226 °C; CIMS m/e calc'd for $C_{27}H_{24}N_3O_5$: 470.1716, found: 470.1739.

Example XV

Preparation of 3-(2-methoxyphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 2-methoxyacetophenone as the starting material. mp 276 °C; CIMS m/e calc'd for $C_{19}H_{16}N_3O_3$: 334.1192, found: 334.1169.

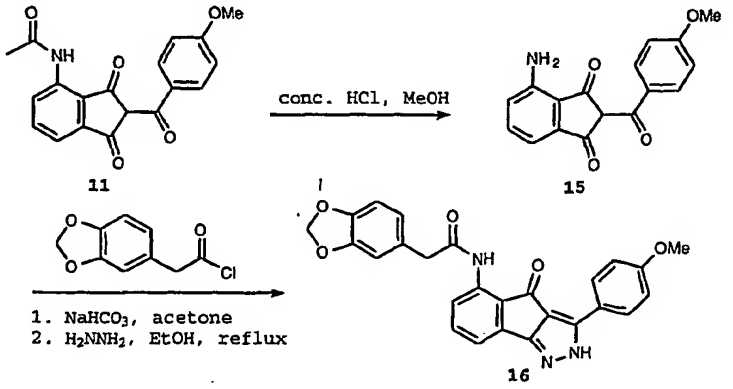
Example XVI

Preparation of 3-(3,4-dimethoxyphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 3,4-dimethoxyacetophenone as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{20}H_{18}N_3O_4$: 364.1297, found: 364.1288.

Example XVII

Preparation of 3-(4-methoxyphenyl)-5-((3,4-ethylenedioxyphenyl)acetamido)indeno[1,2-c]pyrazol-4-one



Step 1. Synthesis of 15 from 11.

A suspension of 11 (5 g, 14.8 mmol) in MeOH (50 mL) was treated with conc. HCl (3 mL) and heated to reflux. After stirring for 2 h, the reaction was cooled to 0 °C and the

product collected as a yellow solid (4.2 g, 96%). mp 173 °C; CIMS m/e calc'd for $C_{17}H_{14}NO_4$: 296.0923, Found: 296.0901.

Step 2. Synthesis of 16 from 15.

A suspension of 15 (20 mg, 0.07 mmol) in acetone (2 mL) was treated with $NaHCO_3$ (10 mg) and the acid chloride of (3,4-methylenedioxyphenyl)acetic acid (prepared by heating the acid in a benzene:thionyl chloride 4:1 mixture at 50 °C for 2 h, removing the volatile components at reduced pressure, and using the crude acid chloride without further purification). The reaction was heated to 50 °C and stirred for 2 h. The reaction was cooled, poured into water (4 mL), extracted with EtOAc (10 mL), dried ($MgSO_4$), filtered and concentrated. The crude triketone was suspended in EtOH (2 mL), treated with hydrazine hydrate (0.05 mL) and p-TsOH (1 mg) and heated to reflux for 2 h. The reaction was cooled to 0 °C and the product filtered to give a yellow solid (6.5 mg, 20%). mp 297 °C; CIMS m/e calc'd for $C_{26}H_{20}N_3O_5$: 454.1403, Found: 454.1398.

Example XVIII

Preparation of 3-(4-dimethoxyphenyl)-5-((3-thiophene)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XVII using the acid chloride of 3-thiopheneacetic acid as the starting material. mp 293 °C; CIMS m/e calc'd for $C_{23}H_{18}N_3O_3S$: 416.1069, found: 416.1088.

Example XIX

Preparation of 3-(4-methoxyphenyl)-5-((2-methoxyphenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XVII using the acid chloride of 2-methoxyphenylacetic acid as the starting material. mp 255 °C; CIMS m/e calc'd for $C_{26}H_{22}N_3O_4$: 440.1610, found: 440.1622.

Example XX

Preparation of 3-(4-methoxyphenyl)-5-((3,4-dichlorophenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XVII using the acid chloride of 3,4-dichlorophenylacetic acid as the starting material. mp 299 °C; CIMS m/e calc'd for $C_{25}H_{18}N_3O_3Cl_2$: 478.0725, found: 478.0744.

Example XXI

Preparation of 3-(4-methoxyphenyl)-5-((2,4-dichlorophenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XVII using the acid chloride of 2,4-dichlorophenylacetic acid as the starting material. mp 286 °C; CIMS m/e calc'd for $C_{25}H_{18}N_3O_3Cl_2$: 478.0725, found: 478.0734.

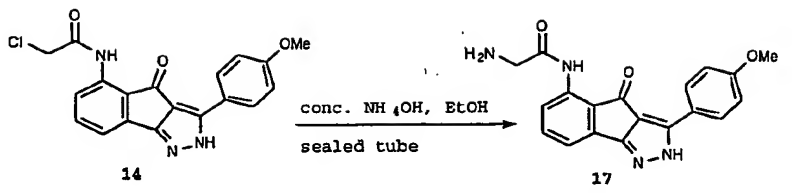
Example XXII

Preparation of 3-(4-methoxyphenyl)-5-((2-chlorophenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XVII using the acid chloride of 2-chlorophenylacetic acid as the starting material. mp 300 °C; CIMS m/e calc'd for $C_{25}H_{19}N_3O_3Cl$: 444.1115, found: 444.1111.

Example XXIII

Preparation of 3-(4-methoxyphenyl)-5-(aminoacetamido)indeno[1,2-c]pyrazol-4-one



14 17

A suspension of 14 (15 mg, 0.04 mmol) in EtOH (1 mL) was treated with conc. NH_4OH (1 mL), placed in a sealed tube and heated to 80 °C for 3 h. The reaction was cooled and the solvent removed at reduced pressure. The residue was recrystallized from EtOH to give the product as a yellow solid (9 mg, 62%). mp >300 °C; CIMS m/e calc'd for $C_{20}H_{19}N_4O_3$: 363.1457, Found: 363.1431.

Example XXIV

Preparation of 3-(4-methoxyphenyl)-5-((2-hydroxyethyl)aminoacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using hydroxylamine as the starting material. mp 243 °C; CIMS m/e calc'd for $C_{21}H_{21}N_4O_4$: 393.1563, found: 393.1539.

Example XXV

Preparation of 3-(4-methoxyphenyl)-5-(N,N-dimethylaminoacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using dimethylamine as the starting material. mp 279 °C; CIMS m/e calc'd for $C_{21}H_{21}N_4O_3$: 377.1614, found: 377.1640.

Example XXVI

Preparation of 3-(4-methoxyphenyl)-5-(piperazinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using piperazine as the starting material. mp 277 ºC; CIMS m/e calc'd for $C_{23}H_{24}N_5O_3$: 418.1879, found: 418.1899.

Example XXVII

Preparation of 3-(4-methoxyphenyl)-5-(4-methylpiperazinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-methylpiperizine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{26}N_5O_3$: 432.2036, found: 432.2030.

Example XXVIII

Preparation of 3-(4-methoxyphenyl)-5-(4-(2-hydroxyethyl)piperazinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-hydroxyethylpiperizine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{28}N_5O_4$: 462.2141, found: 462.2128.

Example XXIX

Preparation of 3-(4-methoxyphenyl)-5-(piperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using piperidine as the starting material. mp 291 °C; CIMS m/e calc'd for $C_{24}H_{25}N_4O_3$: 417.1927, found: 417.1955.

Example XXX

Preparation of 3-(4-methoxyphenyl)-5-(4-aminomethylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-aminomethylpiperidine as the starting

material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{28}N_5O_3$: 446.2192, found: 446.2166.

Example XXXI

Preparation of 3-(4-methoxyphenyl)-5-(ethylaminoacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using ethylamine as the starting material. mp 250 °C; CIMS m/e calc'd for $C_{21}H_{21}N_4O_3$: 377.1614, found: 377.1644.

Example XXXII

Preparation of 3-(4-methoxyphenyl)-5-(thiomorpholinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using thiomorpholine as the starting material. mp 298 °C; CIMS m/e calc'd for $C_{23}H_{23}N_4O_3S$: 435.1491, found: 435.1477.

Example XXXIII

Preparation of 3-(4-methoxyphenyl)-5-(morpholinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using morpholine as the starting material. mp 295 °C; CIMS m/e calc'd for $C_{23}H_{23}N_4O_4$: 419.1719, found: 419.1744.

Example XXXIV

Preparation of 3-(4-methoxyphenyl)-5-(pyrrolidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using pyyrolidine as the starting material. mp 279 °C; CIMS m/e calc'd for $C_{23}H_{23}N_4O_3$: 403.1770, found: 403.1761.

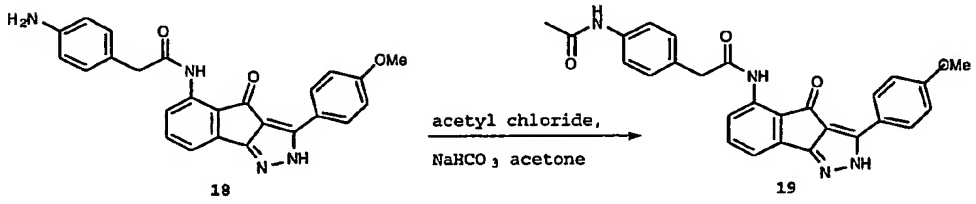
Example XXXV

Preparation of 3-(4-methoxyphenyl)-5-(4-pyridinylaminomethylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-aminomethylpyridine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{22}N_5O_3$: 440.1723, found: 440.1762.

Example XXXVI

Preparation of 3-(4-methoxyphenyl)-5-((4-acetamidophenyl)acetamido)indeno[1,2-c]pyrazol-4-one



A suspension of 18 (10 mg, 0.02 mmol) in dioxane (1 mL) was treated with aqueous sat. $NaHCO_3$ (0.5 mL) and acetyl chloride (0.01 mL) and heated at 50 °C for 1 h. The reaction was cooled, poured into water (5 mL), extracted with EtOAc (10 mL), the organic layer separated, dried ($MgSO_4$) and the solvent removed at reduced pressure. The residue was recrystallized from EtOH to give the product as a yellow solid (5.6 mg, 61%). mp 268 °C; CIMS m/e calc'd for $C_{27}H_{23}N_4O_4$: 467.1719, Found: 467.1730.

Example XXXVII

Preparation of 3-(4-methoxyphenyl)-5-((4-methoxycarbonylaminophenyl)acetamido) indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXXII using methylchloroformate as the starting material. mp 257 °C; CIMS m/e calc'd for $C_{27}H_{23}N_4O_5$: 483.1668, found: 483.1633.

Example XXXVIII

Preparation of 3-(4-methoxyphenyl)-5-((4-aminomethylcarbonylaminophenyl)acetamido) indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII and XXXII using chloroacetyl chloride and conc. NH_4OH as the starting materias. mp 228 °C; CIMS m/e calc'd for $C_{27}H_{24}N_5O_4$: 482.1828, found: 482.1844.

Example XXXIX

Preparation of 3-(4-methoxyphenyl)-5-((4-N,N-dimethylaminomethylcarbonylaminophenyl)acetamido) indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII and XXXII using chloroacetyl chloride and dimethyl amine as the starting materias. mp >300 °C; CIMS m/e calc'd for $C_{29}H_{28}N_5O_4$: 510.2141, found: 510.2121.

Example XL

Preparation of 3-(4-methoxyphenyl)-5-((4-azidophenyl)acetamido)indeno[1,2-c]pyrazol-4-one

A solution of example XXXVI (20 mg, 0.04 mmol) in DMF (2 mL) was treated with 5% palladium on carbon (5 mg) and hydrogentaed at atmospheric pressure using a hydrogen baloon. After 2 h, the solution was filtered (Celite), and the solvent removed at reduced pressure. The residue was recrystallized from EtOH to give the product as a yellow

solid (15 mg, 78%). mp >300 °C; CIMS m/e calc'd for $C_{25}H_{19}N_6O_3$: 451.1519, found: 451.1544.

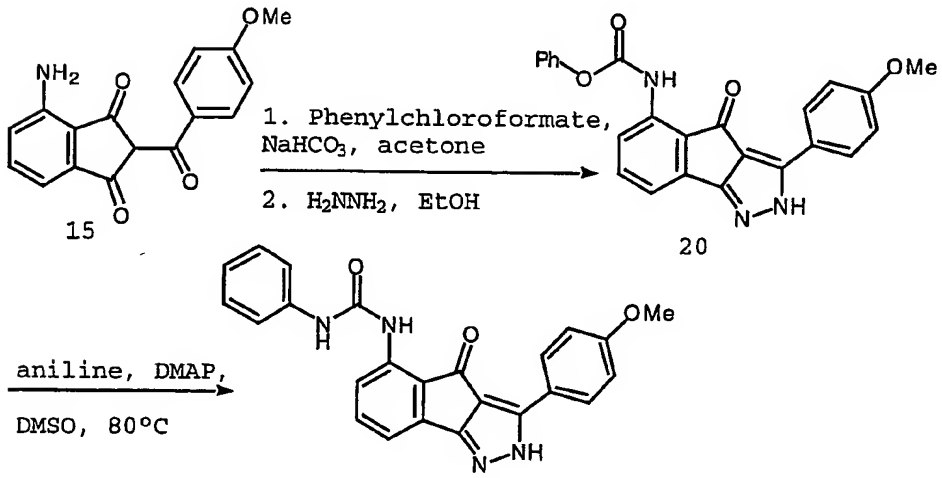
Example XLI

Preparation of 3-(4-methoxyphenyl)-5-((4-aminophenyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXVII using the acid chloride of 4-azidophenylacetic acid as the starting material. mp 283°C; CIMS m/e calc'd for $C_{25}H_{21}N_4O_3$: 425.1614, found: 425.1643.

Example XLII

Preparation of 3-(4-methoxyphenyl)-5-(phenylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one



Step 1. Synthesis of 20 from 15.

A suspension of 15 (0.5 g, 1.7 mmol) in acetone (10 mL) was treated with NaHCO3 (0.5 g) and phenyl chloroformate. The mixture was heated to 50 °C for 2 h. The reaction was

cooled, poured into water (20 mL), extracted with EtOAc (40 mL), the organic layer separated, dried ($MgSO_4$) and the solvent removed at reduced pressure. The residue was suspended in EtOH (10 mL) and treated with hydrazine hydrate (0.16 mL, 5.1 mmol) and p-TsOH (10 mg). The mixture was heated to reflux and stirred for 3 h. The reaction was cooled to 0 °C and the product collected as a yellow solid (0.25 g, 36%). mp 195 °C; CIMS m/e calc'd for $C_{24}H_{18}N_3O_4$: 412.1297, Found: 412.1308.

Step 2. Synthesis of 21 from 20.

A solution of 20 (20 mg, 0.05 mmol) in DMSO (2 mL) was treated with aniline (20 mL, mmol) and dimethylaminopyridine (1 mg). The mixture was heated to 80 °C for 2 h. The reaction was cooled, poured into water (4 mL), extracted with EtOAc (15 mL), the organic layer separated, dried ($MgSO_4$) and the solvent removed at reduced pressure. The residue was recrystallized from EtOH to give the product as a yellow solid (9 mg, 44%). mp >300 °C; CIMS m/e calc'd for $C_{24}H_{19}N_4O_3$: 411.1457, Found: 411.1432.

Example XLIII

Preparation of 3-(4-methoxyphenyl)-5-(butylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using butyl amine as the starting material. mp 252 °C; CIMS m/e calc'd for $C_{21}H_{21}N_4O_3$: 377.1614, found: 377.1633.

Example XLIV

Preparation of 3-(4-methoxyphenyl)-5-(4-aminobenzylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using 4-aminobenzyl amine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{22}N_5O_3$: 440.1723, found: 440.1700.

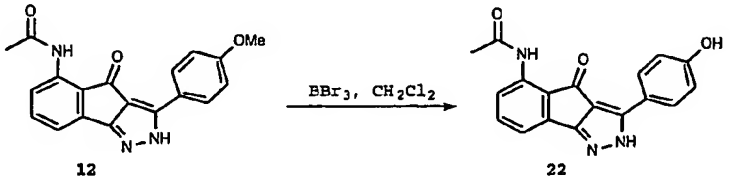
Example XLV

Preparation of 3-(4-methoxyphenyl)-5-(4-pyridylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using 4-aminomethylpyridine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{20}N_5O_3$: 426.1566, found: 426.1533.

Example XLVI

Preparation of 3-(4-hydroxyphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

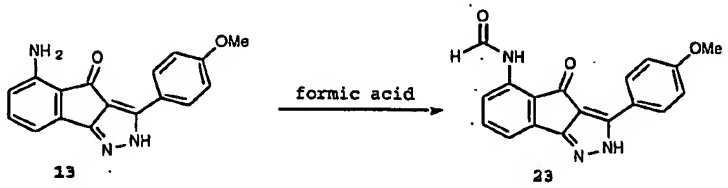


12 22

A suspension of 12 (20 mg, 0.07 mmol) in CH_2Cl_2 (2 mL) was treated with excess BBr_3 (1.0 mL, 1.0 M in CH_2Cl_2) and stirred for 20 h. The reaction was slowly poured into aqueous sat. $NaHCO_3$ (5 mL), extracted with EtOAc (10 mL), dried ($MgSO_4$) and concentrated. The residue was recrystallized from EtOH to give the desired product as a yellow solid (7.5 mg, 33%). mp >300 °C; CIMS m/e calc'd for $C_{18}H_{14}N_3O_3$: 320.1035, Found: 320.1050.

Example XLVII

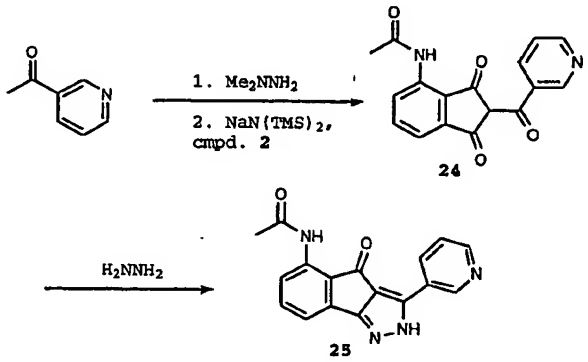
Preparation of 3-(4-methoxyphenyl)-5-(formamido)indeno[1,2-c]pyrazol-4-one



A suspension of 13 (20 mg, 0.06 mmol) in formic acid (2 mL) was heated to 100 °C for 2 h. The reaction mixture was cooled and the solvent removed at reduced pressure. The residue was recrystallized from EtOH to give the desired product as a yellow solid (12 mg, 63%). mp 280 °C; CIMS m/e calc'd for $C_{18}H_{14}N_3O_3$: 320.1035, Found: 320.1040.

Example XLVIII

Preparation of 3-(3-pyridyl)-5-(acetamido)indeno [1,2-c]pyrazol-4-one



Step 1. Synthesis of 24 from 3-acetylpyridine.

A solution of 3-acetylpyridine (1.0 g, 8.3 mmol) in benzene (3 mL) was treated with 1,1-dimethylhydrazine (0.62 mL, 8.3 mmol) and p-TsOH (5 mg). The mixture was heated to 85 °C and stirred for 3 h. The reaction was cooled and the solvent removed at reduced pressure. This crude hydrazone was treated with 1.0 M $NaN(TMS)_2$ in THF (16.6 mL, 16.6 mmol)

at 25 °C over 5 min. After 30 min dimethyl 3-acetamidophthalate (2.1 g, 8.3 mmol) was added in one portion and the reaction heated to reflux. Stirring was continued for 6 h. The reaction was cooled and quenched by the slow addition of TFA. The solvent was removed at reduced pressure and the residue chromatographed (silica, 2.5-5 % MeOH/CH_2Cl_2) to give the product as a yellow solid (0.35 g, 14%). mp 265 °C; CIMS m/e calc'd for $C_{17}H_{13}N_2O_4$: 309.0875, Found: 309.0888.

Step 2. Synthesis of 25 from 24.

A suspension of 24 (30 mg, 0.09 mmol) in EtOH (2 mL) was treated with hydrazine hydrate (0.05 mL) and p-TsOH (1 mg) and heated to reflux. After stirring for 2 h. the reaction was cooled and the product filtered to give a yellow solid (12 mg, 44%). mp >300 °C; CIMS m/e calc'd for $C_{17}H_{13}N_4O_2$: 305.1039, Found: 305.1048.

Example XLIX

Preparation of 3-(4-pyridyl)-5-(acetamido)indeno [1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLVIII using 4-acetylpyridine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{17}H_{13}N_4O_2$: 305.1039, found: 305.1046.

Example L

Preparation of 3-(4-pyridyl)-5-(formamido)indeno [1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLVII using 4-acetylpyridine as the starting material. mp

>300 °C; CIMS m/e calc'd for $C_{16}H_{11}N_4O_2$: 291.0882, found: 291.0882.

Example LI

Preparation of 3-phenyl-5-(acetamido)indeno [1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using acetophenone as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{18}H_{13}N_3O_2$: 304.1065, found: 304.1086.

Example LII

Preparation of 3-(4-methylthiophenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-methylthioacetophenone as the starting material. mp 283 °C; CIMS m/e calc'd for $C_{19}H_{15}N_3O_2S$: 350.0956, found: 350.0963.

Example LIII

Preparation of 3-(4-methylsulphonylphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared by oxidation of the product of example LII. mp >300 °C; CIMS m/e calc'd for $C_{19}H_{15}N_3O_4S$: 382.0860, found: 382.0862.

Example LIV

Preparation of 3-(4-N,N-dimethylaminophenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-N,N,-dimethylaminoacetophenone as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{20}H_{18}N_4O_2$: 347.1496, found: 347.1508.

Example LV

Preparation of 3-(4-N,N-dimethylaminophenyl)-5-(morpholinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LIV and morpholine as the starting materials. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{26}N_5O_3$: 432.2036, found: 432.2020.

Example LVI

Preparation of 3-(4-N,N-dimethylaminophenyl)-5-(dimethylaminoacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LIV and dimethylamine as the starting materials. mp >300 °C; CIMS m/e calc'd for $C_{22}H_{24}N_5O_2$: 390.1930, found: 390.1948.

Example LVII

Preparation of 3-(4-(1-piperidinyl)phenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-(1-piperidinyl)acetophenone as the starting material. mp 291 °C; CIMS m/e calc'd for $C_{23}H_{22}N_4O_2$: 387.1801, found: 387.1821.

Example LVIII

Preparation of 3-(4-morpholinyl)phenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-morpholinylacetophenone as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{22}H_{20}N_4O_3$: 388.1528, found: 388.1535.

Example LIX

Preparation of 3-(4-ethoxyphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-ethoxyacetophenone as the starting material. mp 288 °C; CIMS m/e calc'd for $C_{20}H_{17}N_3O_3$: 348.1325, found: 348.1348.

Example LX

Preparation of 3-(4-butylphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-butylacetophenone as the starting material. mp 259 °C; CIMS m/e calc'd for $C_{22}H_{21}N_3O_2$: 360.1701, found: 360.1712.

Example LXI

Preparation of 3-(4-ethylphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-ethylacetophenone as the starting material. mp 294 °C; CIMS m/e calc'd for $C_{20}H_{17}N_3O_2$: 331.1310, found: 331.1321.

Example LXII

Preparation of 3-(4-n-propylphenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example I using 4'-n-propylacetophenone as the starting material. mp 269 °C; CIMS m/e calc'd for $C_{21}H_{19}N_3O_2$: 346.1555, found: 346.1554.

Example LXIII

Preparation of 3-(4-methoxyphenyl)-5-carbamoylaminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using concentrated ammonium hydroxide as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{18}H_{15}N_4O_3$: 335.1144, found: 335.1113.

Example LXIV

Preparation of 3-(4-methoxyphenyl)-5-(dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using dimethylamino hydrazine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{20}H_{20}N_5O_3$: 378.1566, found: 378.1555.

Example LXV

Preparation of 3-(4-methoxyphenyl)-5-(methylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using methylamine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{19}H_{17}N_4O_3$: 349.1300, found: 349.1311.

Example LXVI

Preparation of 3-(4-methoxyphenyl)-5-(morpholinocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using N-aminomorpholine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{22}H_{22}N_5O_4$: 420.1671, found: 420.1655.

Example LXVII

Preparation of 3-(4-methoxyphenyl)-5-(cis-2-aminocyclohexanylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using cis-1,2-diaminocyclohexane as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{26}N_5O_3$: 432.2035, found: 432.2020.

Example LXVIII

Preparation of 3-(4-methoxyphenyl)-5-(4-methylpiperazinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XLII using (4-amino)methylpiperazine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{23}H_{25}N_6O_3$: 433.1987, found: 433.1999.

Example LXIX

Preparation of 3-(4-methoxyphenyl)-5-(4-uridomethylpiperadinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using example XXX as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{26}H_{29}N_6O_4$: 489.2250, found: 489.2209.

Example LXX

Preparation of 3-(4-methoxyphenyl)-5-(4-(2-pyridyl)piperazinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-(2-pyridyl)piperazine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{28}H_{27}N_6O_3$: 495.2144, found: 495.2111.

Example LXXI

Preparation of 3-(4-methoxyphenyl)-5-(4-(aminoethyl)piperazinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-(aminoethyl)piperazine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{29}N_6O_3$: 461.2300, found: 461.2333.

Example LXXII

Preparation of 3-(4-methoxyphenyl)-5-(4-amidopiperadinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using isonipecotamide as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{26}N_5O_4$: 460.1984, found: 460.1998.

Example LXXIII

Preparation of 3-(4-methoxyphenyl)-5-(4-hydroxypiperadinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-hydroxypiperadine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{25}N_4O_4$: 433.1875, found: 433.1844.

Example LXXIV

Preparation of 3-(4-methoxyphenyl)-5-(4-hydroxmethylypiperadinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-hydroxmethylypiperadine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{27}N_4O_4$: 447.2032, found:447.2002.

Example LXXV

Preparation of 3-(4-methoxyphenyl)-5-(4-amidopiperazinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-amidopiperazine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{25}N_6O_6$: 493.1835, found:493.1802.

Example LXXVI

Preparation of 3-(4-methoxyphenyl)-5-(4-dimethylaminopiperadinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-dimethylaminopiperadine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{26}H_{30}N_5O_5$: 492.2246, found:492.2220.

Example LXXVII

Preparation of 3-(4-methoxyphenyl)-5-(4-aminopiperadinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-aminopiperadine as the starting material. mp >300 °C; CIMS m/e calc'd for $C_{24}H_{26}N_5O_5$: 464.1933, found:464.1975.

Example LXXVIII

Preparation of 3-(4-(dimethylamino)phenyl)-5-((4-methyl-1-piperazinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LIV and 1-methylpiperazine as the starting materials. mp >300 °C; ESI-MS m/e calc'd for $C_{25}H_{29}N_6O_2$: 445.2352, found: 445.2359.

Example LXXIX

Preparation of 3-(4-(dimethylamino)phenyl)-5-((4-amino methyl-1-piperidinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LIV and 4-(aminomethyl)piperidine as the starting materials. ESI-MS m/e calc'd for $C_{26}H_{31}N_6O_2$: 459.2508, found: 459.2508.

Example LXXX

Preparation of 3-(4-(dimethylamino)phenyl)-5-((4-hydroxy-1-piperidinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LIV and 4-hydroxypiperidine as the starting materials. mp 267 °C; ESI-MS m/e calc'd for $C_{25}H_{28}N_5O_3$: 446.2192, found: 446.2206.

Example LXXXI

Preparation of 3-(4-(4-morpholinyl)phenyl)-5-(4-morpholinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LVIII and morpholine as the starting materials. mp 258 °C; ESI-MS m/e calc'd for $C_{26}H_{28}N_5O_4$: 474.2141, found: 474.2151.

Example LXXXII

Preparation of 3-(4-(4-morpholinyl)phenyl)-5-((4-methyl-1-piperazinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LVIII and 1-methylpiperazine as the starting materials. mp 258 °C; ESI-MS m/e calc'd for $C_{27}H_{31}N_6O_3$: 487.2457, found: 487.2447.

Example LXXXIII

Preparation of 3-(4-(4-morpholinyl)phenyl)-5-((4-hydroxy-1-piperidinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LVIII and 4-hydroxypiperidine as the starting materials. mp 245 °C; ESI-MS m/e calc'd for $C_{27}H_{30}N_5O_4$: 488.2298, found: 488.2290.

Example LXXXIV

Preparation of 3-(4-(4-morpholinyl)phenyl)-5-((4-amino methyl-1-piperidinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples II and XXIII employing the product of example LVIII and 4-(aminomethyl)piperidine as the starting materials. mp 240 °C; ESI-MS m/e calc'd for $C_{28}H_{33}N_6O_3$: 501.2614, found: 501.2619.

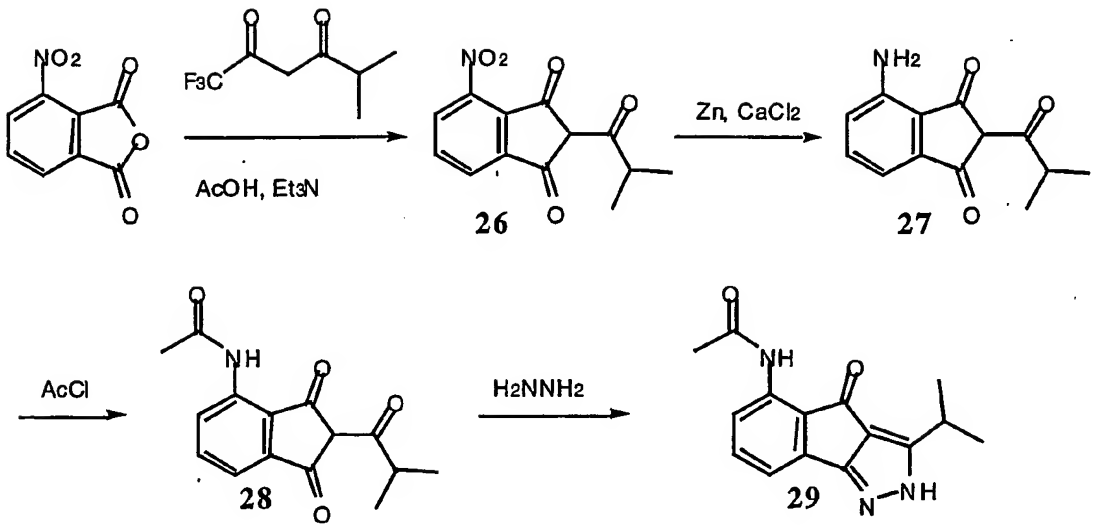
Example LXXXV

Preparation of 3-(4-(dimethylamino)phenyl)-5-((((4-methyl-1-piperazinyl)amino)carbonyl)amino)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples I, XXVII, and XLII employing the 4-(dimethylamino) acetophenone and 1-amino-4-methylpiperazine as the starting materials. mp >300 °C; ESI-MS m/e calc'd for $C_{24}H_{28}N_7O_2$: 446.2304, found: 446.2310.

Example LXXXVI

Preparation of 3-(i-propyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one



Step 1. Synthesis of 26 from 3-nitrophthalic anhydride.

A solution of 3-nitrophthalic anhydride (9.7 g, 50 mmol) and 1,1,1-trifluoro-5-methyl-2,4-hexanedione (9.1 g, 50 mmol) in acetic anhydride (28.3 mL, 300 mmol) was treated with triethylamine (13.95 mL, 100 mmol) and stirred at 25 °C for 4 h. The solution was diluted with 1 N HCl (200 mL) and the precipate collected and washed with water (200 mL) and hexane (400 mL) to give the product as a yellow solid (11.1 g, 85%). mp 127-129 °C; CIMS (M+H) calc'd for $C_{13}H_{12}NO_5$: 262.0715, found: 262.0694.

Step 2. Synthesis of triketone 27 from 26.

A solution of 26 (11 g, 42 mmol) in EtOH (224 mL) and water (56 mL) was treated with zinc (90 g, 1.4 mol) and calcium chloride (3 g, 27 mmol) and heated to reflux for 16 h. The reaction was filtered (Celite) and the filtrate was concentrated at reduced pressure to give an aqueous residue which was extracted with EtOAc (100 mL). The organic layer was separated and washed with sat. EDTA (100 ml) and brine

(100 mL), dried (MgSO4), filtered, and concentrated at reduced pressure to give a yellow solid. Trituration with hexane gave the product as a yellow solid (7.1 g, 73%). mp 241-243 °C; CIMS (M+H) calc'd for $C_{13}H_{14}NO_3$: 232.0974, found: 232.0962.

Step 3. Synthesis of 28 from 27.

A solution of 27 (500 mg, 2.16 mmol) in CH2Cl2 (5 mL) was treated with Et3N (0.36 mL, 2.59 mmol) and stirred at 25 °C for 15 min. The reaction mixture was treated with acetyl chloride (0.18 mL, 2.38 mmol) and stirred at 25 °C for 1 h. The reaction mixture was quenched with 1 N HCl (20 mL) and extracted with EtOAc (20 mL). The organic layer was separated, dried (MgSO4), filtered, and concentrated at reduced pressure to give a brown residue. Trituration with hexane gave the product as a tan solid (484 mg, 82%). mp 241-243 °C; CIMS (M+H) calc'd for $C_{15}H_{16}NO_4$: 274.1079, found: 274.1093.

Step 4. Synthesis of 29 from 28.

A solution of 28 (240 mg, 0.88 mmol) in BuOH (5 mL) was treated with hydrazine hydrate (0.055 mL, 1.76 mmol) and p-TsOH (8.4 mg, 0.044 mmol). The reaction was heated to reflux and stirred for 4 h. The reaction was cooled to 25 °C and the solvent removed at reduced pressure. Recrystalization with i-propyl alcohol gave the product collected as an off-white solid (173 mg, 73%). mp >250 °C; ESIMS (M+H) calc'd for $C_{15}H_{16}N_3O_2$: 270.1242, found: 270.1258.

Example LXXXVII

Preparation of 3-(c-propyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using the c-propyl analog of 26 as the starting material. mp 220-221 °C; CIMS (M+H) calc'd for $C_{15}H_{14}N_3O_2$: 268.1086, found: 268.1078.

Example LXXXVIII

Preparation of 3-(t-butyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using the t-butyl analog of 26 as the starting material. mp >250 °C; CIMS (M+H) calc'd for $C_{16}H_{18}N_3O_2$: 284.1399, found: 284.1395.

Example LXXXIX

Preparation of 3-(2-thienyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using the 2-thienyl analog of 26 as the starting material. mp 269 °C; CIMS (M+H) calc'd for $C_{16}H_{12}N_3O_2S$: 310.0650, found: 310.0635.

Example XC

Preparation of 3-(3-methyl-2-thienyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using the 3-methyl-2-thienyl analog of 26 as the starting material. mp 275 °C; ESIMS (M+H) calc'd for $C_{17}H_{14}N_3O_2S$: 324.0811, found: 324.0807.

Example XCI

Preparation of 3-(ethyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the ethyl analog of 15 as the starting materials. mp >250 °C; CIMS (M+H) calc'd for $C_{13}H_{13}N_4O_2$: 257.1039, found: 257.1033.

Example XCII

Preparation of 3-(n-propyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the n-propyl analog of 15 as the starting materials. mp 187-189 °C; CIMS (M+H) calc'd for $C_{14}H_{15}N_4O_2$: 271.1195, found: 271.1187.

Example XCIII

Preparation of 3-(i-propyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the i-propyl analog of 15 as the starting materials. mp >250 °C; CIMS (M+H) calc'd for $C_{14}H_{15}N_4O_2$: 271.1195, found: 271.1196.

Example XCIV

Preparation of 3-(c-propyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the c-propyl analog of 15 as the starting materials. mp 252-253 °C; ESIMS (M-H) calc'd for $C_{14}H_{11}N_4O_2$: 267.0881, found: 267.0884.

Example XCV

Preparation of 3-(c-hexyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the c-hexyl analog of 15 as the starting materials. mp 178-179 °C; ESIMS (M+H) calc'd for $C_{17}H_{19}N_4O_2$: 311.1507, found: 311.1500.

Example XCVI

Preparation of 3-(2-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 2-thienyl analog of 15 as the starting materials. mp 214 °C; CIMS m+ calc'd for $C_{15}H_{10}N_4O_2S$: 310.0517, found: 310.0524.

Example XCVII

Preparation of 3-(3-methyl-2-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 3-methyl-2-thienyl analog of 15 as the starting materials. mp 270 °C; ESIMS (M+H) calc'd for $C_{16}H_{13}N_4O_2S$: 325.0759, found: 325.0744.

Example XCVIII

Preparation of 3-(5-methyl-2-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 5-methyl-2-thienyl analog of 15 as the starting materials. mp >280 °C; ESIMS (M+H) calc'd for $C_{16}H_{13}N_4O_2S$: 325.0759, found: 325.0761.

Example XCIX

Preparation of 3-(5-ethylcarboxyl-2-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 5-ethylcarboxyl-2-thienyl analog of 15 as the starting materials. mp >280 °C; ESIMS (M+H) calc'd for $C_{18}H_{15}N_4O_4S$: 383.0813, found: 383.0788.

Example C

Preparation of 3-(3-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 3-thienyl analog of 15 as the starting materials. mp >280 °C; ESIMS (M+H) calc'd for $C_{15}H_{11}N_4O_2S$: 311.0603, found: 311.0594.

Example CI

Preparation of 3-(5-chloro-3-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 5-chloro-3-thienyl analog of 15 as the starting materials. mp >300 °C; ESIMS (M+H) calc'd for $C_{15}H_{10}N_4O_2SCl$: 345.0209, found: 345.0213.

Example CII

Preparation of 3-(2,5-dimethyl-3-thienyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 2,5-dimethyl-3-thienyl analog of 15 as the starting materials. mp >280 °C; ESIMS (M+H) calc'd for $C_{17}H_{15}N_4O_2S$: 339.0916, found: 339.0905.

Example CIII

Preparation of 3-(2-furanyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 2-furanyl analog of 15 as the starting materials. mp 278 °C; ESIMS (M+H) calc'd for $C_{15}H_{11}N_4O_3$: 295.0831, found: 295.0838.

Example CIV

Preparation of 3-(i-propyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the i-propyl analog of 15 as the starting materials. mp 231-233 °C; ESIMS (M+H) calc'd for $C_{16}H_{20}N_5O_2$: 314.1616, found: 314.1599.

Example CV

Preparation of 3-(c-propyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the c-propyl analog of 15 as the starting materials. mp XXX °C; ESIMS (M+H) calc'd for $C_{16}H_{18}N_5O_2$: 312.1460, found: 312.1487.

Example CVI

Preparation of 3-(c-hexyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the c-hexyl analog of 15 as the starting materials. mp 229-231 °C; ESIMS (M+H) calc'd for $C_{19}H_{24}N_5O_2$: 354.1929, found: 354.1932.

Example CVII

Preparation of 3-(2-thienyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 2-thienyl analog of 15 as the starting materials. mp 279 °C; ESIMS (M+H) calc'd for $C_{17}H_{16}N_5O_2S$: 354.1024, found: 354.1025.

Example CVIII

Preparation of 3-(5-methoxy-2-thienyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 5-methoxy-2-thienyl analog of 15 as the starting materials. mp 280 °C; ESIMS (M+H) calc'd for $C_{18}H_{18}N_5O_3S$: 384.1130, found: 384.1119.

Example CIX

Preparation of 3-(5-methyl-2-thienyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 5-methyl-2-thienyl analog of 15 as the starting materials. mp >280 °C; ESIMS (M+H) calc'd for $C_{18}H_{18}N_5O_2S$: 368.1181, found: 368.1171.

Example CX

Preparation of 3-(5-ethylcarboxyl-2-thienyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 5-ethylcarboxyl-2-thienyl analog of 15 as the starting materials. mp 252 °C; ESIMS (M+H) calc'd for $C_{20}H_{20}N_5O_4S$: 426.1236, found: 426.1251.

Example CXI

Preparation of 3-(3-thienyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 3-thienyl analog of 15 as the starting materials. mp 202 °C; ESIMS (M+H) calc'd for $C_{17}H_{16}N_5O_2S$: 354.1025, found: 354.1031.

Example CXII

Preparation of 3-(1-methyl-3-pyrrolyl)-5-(carbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using ammonia and the 1-methyl-3-pyrrolyl analog of 15 as the starting materials. mp >300 °C; ESIMS (M+H) calc'd for $C_{16}H_{14}N_5O_2$: 308.1147, found: 308.1166.

Example CXIII

Preparation of 3-(2,5-dimethyl-3-thienyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 2,5-dimethyl-3-thienyl analog of 15 as the starting materials. mp 252 °C; ESIMS (M+H) calc'd for $C_{19}H_{20}N_5O_2S$: 382.1338, found: 382.1357.

Example CXIV

Preparation of 3-(2-furanyl)-5-(N,N-dimethylaminocarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1,1-dimethylhydrazine and the 2-furanyl analog of 15 as the starting materials. mp 202 °C; ESIMS (M+H) calc'd for $C_{17}H_{16}N_5O_3$: 338.1253, found: 338.1248.

Example CXV

Preparation of 3-(i-propyl)-5-(4-carbamoylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using isonipecotamide and the i-propyl analog of 14 as the starting materials. mp 224-225 °C; ESIMS (M+H) calc'd for $C_{21}H_{26}N_5O_3$: 396.2035, found: 396.2036.

Example CXVI

Preparation of 3-(c-hexyl)-5-(4-carbamoylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using isonipecotamide and the c-hexyl analog of 14 as the starting materials. mp 228-229 °C; ESIMS (M+H) calc'd for $C_{24}H_{30}N_5O_3$: 436.2348, found: 436.2345.

Example CXVII

Preparation of 3-(ethyl)-5-(4-aminomethylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-(aminomethyl)piperidine and the ethyl analog of 14 as the starting materials. mp 174-176 °C; ESIMS (M+H) calc'd for $C_{20}H_{26}N_5O_2$: 368.2086, found: 368.2078.

Example CXVIII

Preparation of 3-(i-propyl)-5-(4-aminomethylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-(aminomethyl)piperidine and the i-propyl analog of 14 as the starting materials. mp 218-220 °C; ESIMS (M+H) calc'd for $C_{21}H_{28}N_5O_2$: 382.2242, found: 382.2227.

Example CXIX

Preparation of 3-(c-propyl)-5-(4-aminomethylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-(aminomethyl)piperidine and the c-propyl analog of 14 as the starting materials. mp 138-140 °C; ESIMS (M+H) calc'd for $C_{21}H_{26}N_5O_2$: 380.2086, found: 380.2079.

Example CXX

Preparation of 3-(c-hexyl)-5-(4-aminomethylpiperidinylacetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example XXIII using 4-(aminomethyl)piperidine and the c-hexyl analog of 14 as the starting materials. mp 196-198 °C; ESIMS (M+H) calc'd for $C_{24}H_{32}N_5O_2$: 422.2555, found: 422.2540.

Example CXXI

Preparation of 3-(i-propyl)-5-(4-methylpiperazinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1-amino-4-methylpiperazine and the i-propyl analog of 15 as the starting materials. mp 231-233 °C; ESIMS (M+H) calc'd for $C_{19}H_{25}N_6O_2$: 369.2038, found: 369.2039.

Example CXXII

Preparation of 3-(5-ethylcarboxyl-2-thienyl)-5-(4-methylpiperazinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1-amino-4-methylpiperazine and the 5-ethylcarboxyl-2-thienyl analog of 15 as the starting

materials. mp 249 °C; ESIMS (M+H) calc'd for $C_{23}H_{25}N_6O_4S$: 481.1657, found: 481.1642.

Example CXXIII

Preparation of 3-(5-carboxyl-2-thienyl)-5-(4-methylpiperazinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

A solution of CXXII (30 mg, 0.05 mmol) in 3:1 THF/water (2 mL) was treated with LiOH (23 mg, 0.5 mmol) and the reaction was stirred at 25 °C for 12 h and then heated to reflux for 1 h. The organic solvent was removed at reduced pressure and the residue was partioned between EtOAc (5 mL) and water (5 mL). The organic layer was separated and the aqueous phase was adjusted to pH = 2 with 1 M HCl and re-extracted with EtOAc (5 mL). The combined organic layers were dried (Na2SO4), filtered and concentrated at reduced pressure to give a crude residue. Purification by reverse phase HPLC gave the product as a yellow solid (10.4 mg, 46%). mp 270 °C; ESIMS (M+H) calc'd for $C_{21}H_{21}N_6O_4S$: 453.1344, found: 453.1353.

Example CXXIV

Preparation of 3-(2,5-dimethyl-3-thienyl)-5-(4-methylpiperazinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 1-amino-4-methylpiperazine and the 2,5-dimethyl-3-thienyl analog of 15 as the starting materials. mp 250 °C; ESIMS (M+H) calc'd for $C_{22}H_{25}N_6O_2S$: 437.1760, found: 437.1771.

Example CXXV

Preparation of 3-(i-propyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 4-aminomorpholine and the i-propyl analog of 15 as the starting materials. mp 256-258 °C; ESIMS (M-H) calc'd for $C_{18}H_{20}N_5O_3$: 354.1566, found: 354.1543.

Example CXXVI

Preparation of 3-(N-methylcarbamoyl-4-piperidinyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 4-aminomorpholine and the N-methylcarbamoyl-4-piperidinyl analog of 15 as the starting materials. mp 216-218 °C; ESIMS (M+H) calc'd for $C_{22}H_{27}N_6O_5$: 455.2042, found: 455.2036.

Example CXXVII

Preparation of 3-(5-methyl-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 4-aminomorpholine and the 5-methyl-2-thienyl analog of 15 as the starting materials. mp 261 °C; ESIMS (M+H) calc'd for $C_{20}H_{20}N_5O_3S$: 410.1287, found: 410.1308.

Example CXXVIII

Preparation of 3-(5-chloro-3-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 4-aminomorpholine and the 5-chloro-3-thienyl analog of 15 as the starting materials. mp 259 °C; ESIMS (M+H) calc'd for $C_{19}H_{17}N_5O_3SCl$: 430.0741, found: 430.0757.

Example CXXIX

Preparation of 3-(2,5-dimethyl-3-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 4-aminomorpholine and the 2,5-dimethyl-3-thienyl analog of 15 as the starting materials. mp >280 °C; ESIMS (M+H) calc'd for $C_{21}H_{22}N_5O_3S$: 424.1443, found: 424.1431.

Example CXXX

Preparation of 3-(5-ethylcarboxyl-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI using 4-aminomorpholine and the 5-ethylcarboxyl-2-thienyl analog of 15 as the starting materials. mp 258 °C; ESIMS (M+H) calc'd for $C_{22}H_{22}N_5O_5S$: 468.1341, found: 468.1331.

Example CXXXI

Preparation of 3-(5-carboxyl-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI (HYDROLYSIS OF PREVIOUS ESTER). mp 273 °C; ESIMS (M+H) calc'd for $C_{20}H_{18}N_5O_5S$: 440.1028, found: 440.1026.

Example CXXXII

Preparation of 3-(5-benzylcarboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

A solution of benzylamine (0.01 mL, 0.09 mmol) in DMF (1 mL) was treated with acid CXXXI (40 mg, 0.09 mmol) and stirred at 25 °C. The reaction was treated with TBTU (29 mg, 0.09 mmol) and stirred at 25 °C for 30 min. Triethylamine (0.01 mL, 0.09 mmol) was added and the reaction stirred at

25 °C for 12 h. After adding more TBTU (15 mg, 0.045 mmol) and triethylamine (0.01 mL, 0.09 mmol) the reaction was stirred at 25 °C for an additional 4 h. The reaction was diluted with EtOAc (10 mL) and water (10 mL) and the aqueous layer was extracted with EtOAc (5 x 10 mL). The combined organic layers were dried (Na2SO4), filtered, and the solvent removed at reduced pressure. Purification of the residue using reverse phase HPLC gave the product as a yellow solid (21 mg, 42%). mp 275 °C; ESIMS (M+H) calc'd for $C_{27}H_{25}N_5O_4S$: 529.1659, found: 529.1682.

Example CXXXIII

Preparation of 3-(5-(4-methylpiperazinyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 1-amino-4-methylpiperazine as the starting material. mp 190 °C; ESIMS (M+H) calc'd for $C_{25}H_{29}N_8O_4S$: 537.2032, found: 537.2055.

Example CXXXIV

Preparation of 3-(5-(2-(1-methylpyrrolidinyl)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 2-(2-aminoethyl)-1-methylpyrrolidine as the starting material. mp 235 °C; ESIMS (M+H) calc'd for $C_{27}H_{32}N_7O_4S$: 550.2236, found: 550.2229.

Example CXXXV

Preparation of 3-(5-(N,N-dimethylamino)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 1,1-dimethylhydrazine as the starting material. mp 201 °C; ESIMS (M+H) calc'd for $C_{22}H_{24}N_7O_4S$: 482.1610, found: 482.1588.

Example CXXXVI

Preparation of 3-(5-(2-(N,N-dimethylamino)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using N,N-dimethylethylenediamine as the starting material. mp 190 °C; ESIMS (M+H) calc'd for $C_{24}H_{28}N_7O_4S$: 510.1923, found: 510.1922.

Example CXXXVII

Preparation of 3-(5-(2-(pyrrolidinyl)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 1-(2-aminoethyl)pyrrolidine as the starting material. mp 224 °C; ESIMS (M+H) calc'd for $C_{26}H_{30}N_7O_4S$: 536.2080, found: 536.2091.

Example CXXXVIII

Preparation of 3-(5-(2-(morpholinyl)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 4-(2-aminoethyl)morpholine as the starting

material. mp 241 °C; ESIMS (M+H) calc'd for $C_{26}H_{30}N_7O_5S$: 552.2029, found: 552.2043.

Example CXXXIX

Preparation of 3-(5-morpholinylcarboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 4-aminomorpholine as the starting material. mp 271 °C; ESIMS (M+H) calc'd for $C_{24}H_{26}N_7O_5S$: 524.1716, found: 524.1719.

Example CXL

Preparation of 3-(5-(3-(pyrrolidonyl)propyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 1-(3-aminopropyl)-2-pyrrolidinone as the starting material. mp 260 °C; ESIMS (M+H) calc'd for $C_{27}H_{30}N_7O_5S$: 564.2029, found: 564.2031.

Example CXLI

Preparation of 3-(5-(2-(3-pyridyl)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 3-(2-aminoethyl)pyridine as the starting material. mp 203 °C; ESIMS (M+H) calc'd for $C_{27}H_{26}N_7O_4S$: 544.1766, found: 544.1760.

Example CXLII

Preparation of 3-(5-(3-(imidazolyl)propyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 1-(3-aminopropyl)imidazole as the starting material. mp 263 °C; ESIMS (M+H) calc'd for $C_{26}H_{27}N_8O_4S$: 547.1875, found: 547.1872.

Example CXLIII

Preparation of 3-(5-(2-(2-pyridyl)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 2-(2-aminoethyl)pyridine as the starting material. mp >280 °C; ESIMS (M+H) calc'd for $C_{27}H_{26}N_7O_4S$: 544.1767, found: 544.1778.

Example CXLIV

Preparation of 3-(5-((2-pyridyl)methyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 2-(aminomethyl)pyridine as the starting material. mp 239 °C; ESIMS (M+H) calc'd for $C_{26}H_{24}N_7O_4S$: 530.1610, found: 530.1603.

Example CXLV

Preparation of 3-(5-(2-(piperidinyl)ethyl)carboxamido-2-thienyl)-5-(morpholinylcarbamoyl)aminoindeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CXXXII using 1-(2-aminoethyl)piperidine as the starting

material. mp 228 °C; ESIMS (M+H) calc'd for $C_{27}H_{32}N_7O_4S$: 550.2236, found: 550.2236.

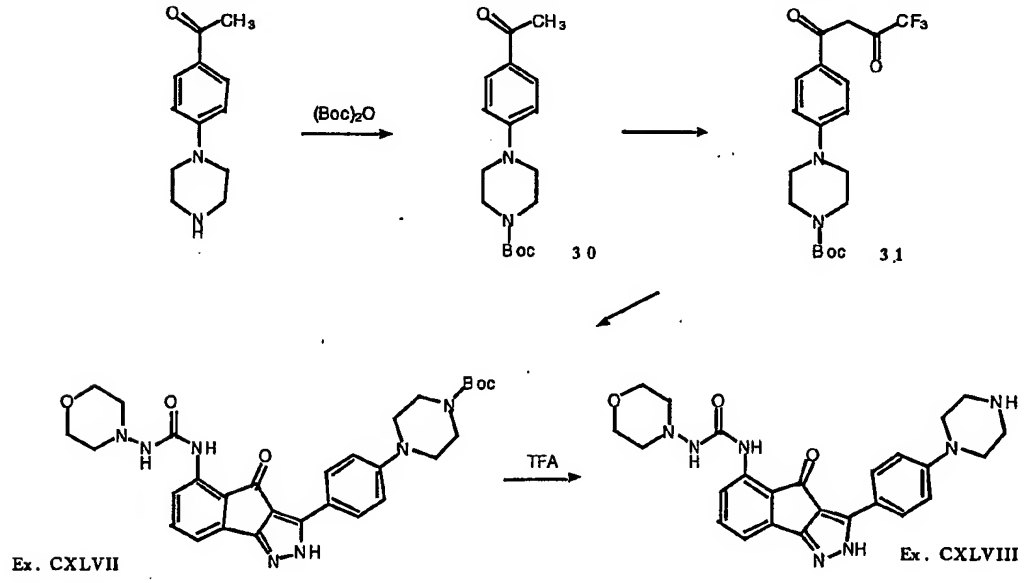
Example CXLVI

Preparation of 3-(4-(trifluoromethyl)phenyl)-5-(acetamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example LXXXVI employing 1-(4-(trifluoromethyl)phenyl)-4,4,4-trifluoro-1,3-butanedione as the starting material. mp >300 °C; ESI$^-$-MS m/e calc'd for $C_{19}H_{11}N_3O_2$: 370.0804, found: 370.0809.

Example CXLVII

Preparation of 3-(4-(4-t-butoxycarbonyl-1-piperazinyl)phenyl)-5-(((4-morpholinylamino)carbonyl)amino)indeno[1,2-c]pyrazol-4-one



Step 1. Synthesis of 30.

A solution of 4-piperazinoacetophenone (24.8 g, 121 mmol) and di-tert-butyl dicarbonate (27.8 g, 128 mmol) in

480 mL of tetrahydrofuran was refluxed for 16 h. After cooling to room temperature the solution was concentrated under vacuum. The resulting solids were washed with hexane and dried under vacuum to afford 29.4 g (80%) of the product as an off-white solid. NMR ($CDCl_3$) δ 7.89 (d, 2 H, J = 9 Hz), 6.87 (d, 2 H, J = 9 Hz), 3.59 (m, 4 H), 3.33 (m, 4 H), 2.53 (s, 3 H), 1.49 (s, 9 H).

Step 2. Synthesis of 31 from 30.

To a solution of 30 (11.35 g, 37 mmol) and ethyl trifluoroacetate (5.40 mL, 45 mmol) in 50 mL of tetrahydrofuran at 25 °C was added dropwise over 15 min. 21% sodium ethoxide in ethanol (16.8 mL, 45 mmol), and the resulting solution then was stirred at 25 °C for 14 h. The reaction mixyure was diluted with water, adjusted to pH 5 with conc. hydrochloric acid, and extracted with ethyl acetate. The combined extracts was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated under vacuum. The resulting solid was washed with diethyl ether and dried to furnish 12.1 g (81%) of the product as an orange solid. NMR ($CDCl_3$) δ 7.87 (d, 2 H, J = 9 Hz), 6.87 (d, 2 H, J = 9 Hz), 6.45 (s, 1 H), 3.60 (m, 4 H), 3.41 (m, 4 H), 1.48 (s, 9 H).

Step 3. Synthesis of CXLVII from 31.

Prepared in a similar fashion as described for examples LXXVI and XLII employing 31 and 4-aminomorpholine as starting materials. mp 242 °C; ESI-MS m/e calc'd for $C_{30}H_{36}N_7O_5$574.2778, found: 574.2762.

Example CXLVIII

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-(((4-morpholinylamino)carbonyl)amino)indeno[1,2-c]pyrazol-4-one

A solution of CXLVII (0.58 g, 1.0 mmol) in 20 mL of trifluoroacetic acid was stirred at 25 °C for 2 h. The reaction mixture was concentrated under vacuum, and the

residue was recrystallized from ethanol to provide 0.53 g (89%) of the yellow product as its TFA-salt. mp 263 °C; ESI-MS m/e calc'd for $C_{25}H_{28}N_7O_3$: 474.2254, found: 474.2280.

Example CXLIX

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-((aminocarbonyl)amino)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples XLII and CXLVIII employing 2-(4-(4-t-butoxycarbonyl-1-piperazinyl)benzoyl)-4-amino-1,3-indanedione obtained in example CXLVII and ammonia as the starting materials. mp 257 °C; ESI-MS m/e calc'd for $C_{21}H_{21}N_6O_2$: 389.1726, found: 389.1724.

Example CL

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-((hydrazinocarbonyl)amino)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for examples XLII and CXLVIII employing 2-(4-(4-t-butoxycarbonyl-1-piperazinyl)benzoyl)-4-amino-1,3-indanedione obtained in example CXLVII and hydrazine as the starting materials. mp 257 °C; ESI-MS m/e calc'd for $C_{21}H_{22}N_7O_2$: 404.1835, found: 404.1834.

Example CLI

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-((dimethylamino)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared employing 2-(4-(4-t-butoxycarbonyl-1-piperazinyl)benzoyl)-4-amino-1,3-indanedione obtained in example CXLVII as the starting material. Chloroacetylation and treatment with dimethylamine in a similar fashion as described for examples II and XXIII, followed by treatment

with hydrazine and removal of the t-butoxycarbonyl group in a similar fashion as described for examples I and CXLVIII, afforded the example compound. mp 243 °C; ESI-MS m/e calc'd for $C_{24}H_{27}N_6O_2$: 431.2196, found: 431.2198.

Example CLII

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-((4-morpholinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared employing 2-(4-(4-t-butoxycarbonyl-1-piperazinyl)benzoyl)-4-amino-1,3-indanedione obtained in example CXLVII as the starting material. Chloroacetylation and treatment with morpholine in a similar fashion as described for examples II and XXIII, followed by treatment with hydrazine and removal of the t-butoxycarbonyl group in a similar fashion as described for examples I and CXLVIII, afforded the example compound. mp 259 °C; ESI-MS m/e calc'd for $C_{26}H_{29}N_6O_3$: 473.2301, found: 473.2302.

Example CLIII

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-((4-methyl-1-piperazinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared employing 2-(4-(4-t-butoxycarbonyl-1-piperazinyl)benzoyl)-4-amino-1,3-indanedione obtained in example CXLVII as the starting material. Chloroacetylation and treatment with 1-methylpiperazine in a similar fashion as described for examples II and XXIII, followed by treatment with hydrazine and removal of the t-butoxycarbonyl group in a similar fashion as described for examples I and CXLVIII, afforded the example compound. ESI-MS m/e calc'd for $C_{27}H_{32}N_7O_2$: 486.2618, found: 486.2608.

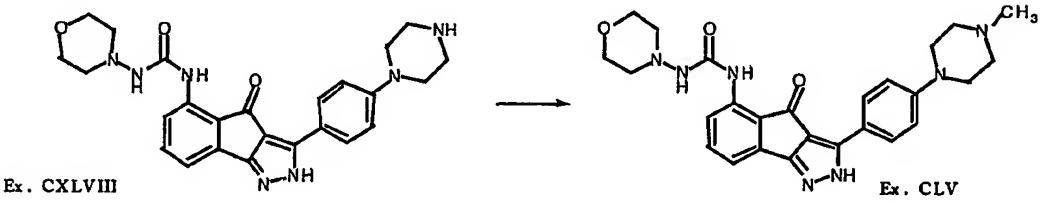
Example CLIV

Preparation of 3-(4-(1-piperazinyl)phenyl)-5-((4-amino methyl-1-piperidinyl)acetamido)indeno[1,2-c]pyrazol-4-one

Prepared employing 2-(4-(4-t-butoxycarbonyl-1-piperazinyl)benzoyl)-4-amino-1,3-indanedione obtained in example CXLVII as the starting material. Chloroacetylation and treatment with 4-(aminomethyl)piperidine in a similar fashion as described for examples II and XXIII, followed by treatment with hydrazine and removal of the t-butoxycarbonyl group in a similar fashion as described for examples I and CXLVIII, afforded the example compound. mp 239 °C; ESI-MS m/e calc'd for $C_{28}H_{34}N_7O_2$: 500.2774, found: 500.2772.

Example CLV

Preparation of 3-(4-(4-methyl-1-piperazinyl)phenyl)-5-(((4-morpholinylamino)carbonyl)amino)indeno[1,2-c]pyrazol-4-one



Ex. CXLVIII Ex. CLV

To a solution of CXLVIII (0.17 g, 0.29 mmol) in 10 mL of methanol and 2 mL of water at 25 °C was added sequentially 37% aqueous formaldehyde (0.45 g, 5.8 mmol), sodium cyanoborohydride (0.18 g, 2.9 mmol), and 4 drops of acetic acid. The resulting solution was stirred at 25 °C for 16 h. The mixture was diluted with water. It then was made acidic (~pH 1) with conc. hydrochloric acid and stirred for 10 min. The solution next was made basic (~pH 13) with 50% aqueous sodium hydroxide and finally adjusted to pH 10 with 1 N hydrochloric acid. The mixture was extracted with 4:1 chloroform/isopropanol. The combined extracts were washed

with water and brine, dried over anhydrous sodium sulfate, and filtered. To the filtrate was added excess trifluoroacetic acid, and the solution was concentrated under vacuum. The residue was recrystallized from isopropanol to furnish 0.16 g (92%) of the yellow product as its TFA-salt. mp 245 °C; ESI-MS m/e calc'd for $C_{26}H_{30}N_7O_3$: 488.2410, found: 488.2420.

Example CLVI

Preparation of 3-(4-(4-ethyl-1-piperazinyl)phenyl)-5-(((4-morpholinylamino)carbonyl)amino)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLV employing CXLVIII and acetaldehyde as the starting materials. mp 245 °C; ESI-MS m/e calc'd for $C_{27}H_{32}N_7O_3$: 502.2567, found: 502.2555.

Example CLVII

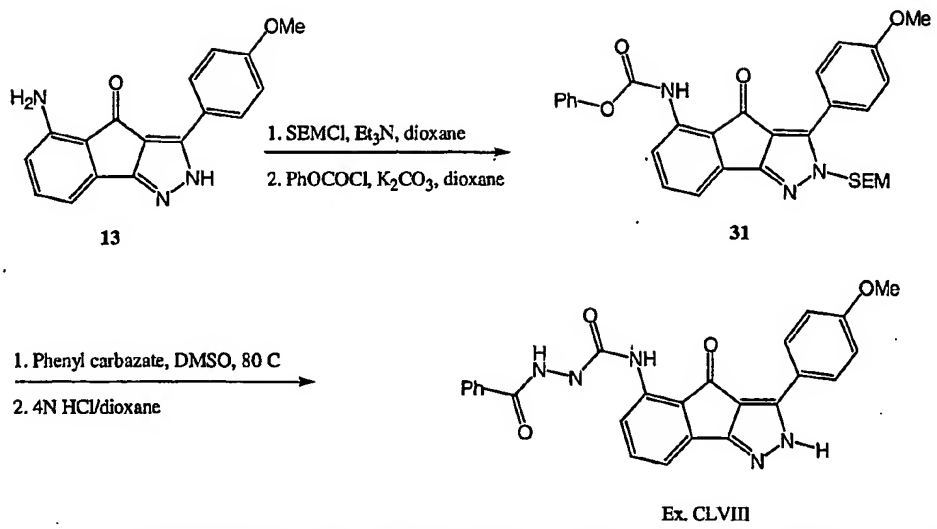
Preparation of 3-(4-(4-isopropyl-1-piperazinyl)phenyl)-5-(((4-morpholinylamino)carbonyl)amino)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLV employing CXLVIII and acetone as the starting materials. mp 253 °C; ESI-MS m/e calc'd for $C_{28}H_{34}N_7O_3$: 516.2723, found: 516.2726.

Example CLVIII

Preparation of 3-(4-methoxyphenyl)-5-(2-benzoylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Step 1. Synthesis of 31 from 13.



Ex. CLVIII

A suspension of aniline 31 (0.5 g, 1.7 mmol) in dioxane (10 mL) was treated with triethylamine (0.48 mL, 3.4 mmol) in one portion at room temperature. Then 2-(trimethylsilyl) ethyloxy chloride (SEMCl) (0.48 mL, 2.6 mmol) was added in one portion and the mixture heated to reflux for 2 h. The reaction was cooled, diluted with EtOAc (20 mL) washed with water (10 mL), dried (MgSO4) and the solvent removed at reduced pressure. The residue was taken up in benzene (3 mL), applied to a plug of silica gel (10 g) and eluted with EtOAc/Hexane (1:3) until all the yellow color was washed from the silica gel plug. The solvent was evaporated and the residue taken on to the next step. This material was dissolved in dioxane (10 mL) and treated with K2CO3 (0.36 g, 2.6 mmol) in one portion. Then phenylchloroformate (0.27 mL, 2.23 mmol) was added in one portion and the reaction heated to 50 C for 2 h. The reaction was cooled and the solvent removed at reduced pressure. The residue was recrystalized from EtOH to give a yellow solid (0.4 g, 43%). mp °C; CIMS m/e calculated for $C_{30}H_{32}N_3O_5Si$: 542.2111, found: 542.2101;

Step 2. Synthesis of Ex. CLVIII from 31.

Compound 31 (0.015 g, 0.03 mmol) in DMSO (0.2 mL) was treated with phenylcarbazte (0.008 g, 0.06 mmol) in one portion and heated to 80 C for 30 minutes. The solvent was removed at reduced pressure heating to 65 C. The residue was disolved in EtOH (0.5 mL) and treated with 4N HCl/dioxane (0.4 mL). The mixture was heated to 80 C for 20 minutes and then cooled. The desired product was filtered and air dried (0.008g, 62%). mp >300 °C; CIMS m/e calculated for $C_{26}H_{27}N_4O_4$: 459.2032, found: 459.1999;

Example CLIX

Preparation of 3-(4-methoxyphenyl)-5-(2-isonicotinoylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 4-pyridylcarbazate as the starting material. mp 248 °C; CIMS m/e calculated for $C_{24}H_{19}N_6O_4$: 455.1468, found: 455.1400;

Example CLX

Preparation of 3-(4-methoxyphenyl)-5-(2-nictinoylhydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 3-pyridylcarbazate as the starting material. mp 227 °C; CIMS m/e calc'd for $C_{24}H_{19}N_6O_4$: 455.1468, found: 455.1487;

Example CLXI

Preparation of 3-(4-methoxyphenyl)-5-(2-(3,4-dihydroxy benzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 3,4-dihydroxyphenyl carbazate as the starting

material. mp >300 °C; CIMS m/e calc'd for $C_{25}H_{20}N_5O_6$: 486.1414, found: 486.1497;

Example CLXII

Preparation of 3-(4-methoxyphenyl)-5-(2-(4-hydroxy benzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 4-hydroxyphenyl carbazate as the starting material. mp 283 °C; CIMS m/e calc'd for $C_{25}H_{20}N_5O_5$: 470.1464, found: 470.1544;

Example CLXIII

Preparation of 3-(4-methoxyphenyl)-5-(2-(3-aminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 3-aminophenyl carbazate as the starting material. mp 250 °C; CIMS m/e calc'd for $C_{25}H_{21}N_6O_4$: 469.1624, found: 469.1513;

Example CLXIV

Preparation of 3-(4-methoxyphenyl)-5-(2-(4-aminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 4-aminophenyl carbazate as the starting material. mp 247 °C; CIMS m/e calc'd for $C_{25}H_{21}N_6O_4$: 469.1624, found: 469.1528;

Example CLXV

Preparation of 3-(4-methoxyphenyl)-5-(2-(2-aminobenzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 2-aminophenyl carbazate as the starting

material. mp 257 °C; CIMS m/e calc'd for $C_{25}H_{21}N_6O_4$: 469.1624, found: 469.1548;

Example CLXVI

Preparation of 3-(4-methoxyphenyl)-5-(2-(4-N,N-dimethylamino benzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 4-N,N-dimethylaminophenyl carbazate as the starting material. mp 259 °C; CIMS m/e calc'd for $C_{27}H_{25}N_6O_4$: 497.1937, found: 497.1876;

Example CLXVII

Preparation of 3-(4-methoxyphenyl)-5-(2-phenethylacetyl hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using benzyl carbazate as the starting material. mp 269 °C; CIMS m/e calc'd for $C_{26}H_{22}N_5O_4$: 468.1672, found: 468.1313;

Example CLXVIII

Preparation of 3-(4-methoxyphenyl)-5-(2-(2-hydroxy benzoyl)hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using 2-hydroxyphenyl carbazate as the starting material. mp 280 °C; CIMS m/e calc'd for $C_{25}H_{20}N_5O_5$: 470.1464, found: 470.1419;

Example CLXIX

Preparation of 3-(4-methoxyphenyl)-5-(2-methoxycarbonyl hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one

Prepared in a similar fashion as described for example CLVIII using carbazic acid methyl ester as the starting

material. mp >300 °C; CIMS m/e calc'd for $C_{20}H_{28}N_5O_5$: 408.1308, found: 408.1397;

EXAMPLE CLXX

Preparation of Intermediate CLXX

The preparation of intermediate CLXX, (N-[2-(4-Methoxy-benzoyl)-1,3-dioxo-indan-4-yl]-acetamide) is described in Nugiel, D.A.; Etzkorn, A.M.; Vidwans, A.; Benfield, P.A.; Boisclair, M.; Burton, C.R.; Cox, S.; Czerniak, P.M.; Doleniak, D.; Seitz, S.P. J. Med. Chem. 2001, 44, 1334-1336 which is herein incorporated by reference in it's entirety as though set forth in full.

EXAMPLE CLXXI

Preparation of Intermediate CLXXI

Synthesis of 4-Amino-2-(4-methoxy-benzoyl)-indan-1,3-dione: The compound prepared in example 1 (2.0 g, 5.93 mmol) is dissolved in 20% HCl in methanol (50 mL). This solution is stirred at reflux for a period of 3 h. It is then allowed to cool to room temperature and stirred overnight. The product is filtered off, washed with ethanol (20 mL) and air dried to give the product as a yellow solid (1.5 g, 85.7%). mp 268-269 °C; ^{1}H NMR ($DMSOd_6$) δ 8.17 (d, J = 8.8 Hz, 2H), 7.49 (t, 1H), 7.12 (d, J = 8.7 Hz, 2H), 6.98 (m, 2H), 3.88 (s, 1H).

EXAMPLE CLXXII

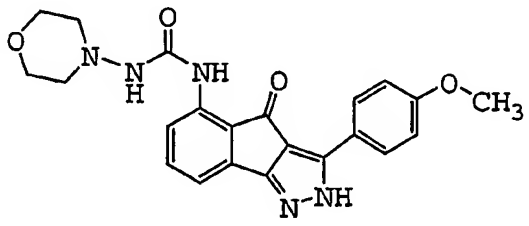
Preparation of Intermediate CLXXII

Synthesis of [2-(4-Methoxybenzoyl)-1,3-dioxo-indan-4-yl]-carbamic acid phenyl ester: The product prepared in Example CLXXI (1.5 g, 5.08 mmol) is dissolved in acetone (40 mL) and treated with sodium carbonate (1.26 g, 15.24 mmol)

and phenyl chloroformate (1.19 g, 7.62 mmol). The suspension is stirred at 50 °C for 3 h. The reaction mixture is diluted with water (120 mL), and extracted with ethyl acetate (2 x 100 mL). The organic layer is separated, washed with brine (50 mL), dried (Na_2SO_4) and the solvent removed at reduced pressure to give a gummy orange residue. Cold ethyl ether (100 mL) is added to this residue to give a precipitate. The precipitate is collected and washed with ethyl ether (2 x 10 mL) to give desired product as a yellow solid (1.65 g. 78%). mp 256-258 °C; ^{1}HNMR (DMSOd_6) δ 10.83 (s, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 2.9 Hz, 2H), 7.54 (m, 3H), 7.28 (m, 3H), 7.09 (t, 1H), 6.89 (d, J = 10.8 Hz, 2H), 3.81 (s, 3H) .

EXAMPLE CLXXIII

Preparation of 1-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-3-morpholin-4-yl-urea

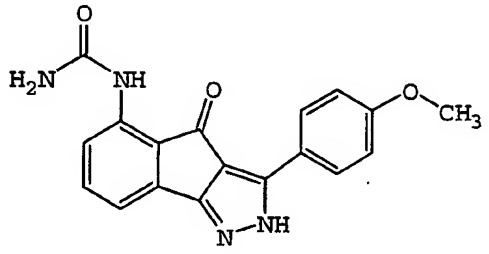


The product prepared in Example CLXXII (0.03 g, 0.072 mmol) in anhydrous DMSO (2 mL) is treated with 4-aminomorpholine (0.0084g, 0.082 mmol) and 4-dimethylaminopyridine (0.005 g, 0.04 mmol) and heated to 80 °C for 3h. The solvent is removed under reduced pressure and the residue triturated with ethanol to give a dark solid. The solid is collected and washed with ethanol (5 mL) to give a tricarbonyl urea (0.03 g, 100%). The tricarbonyl urea

intermediate (0.03 g, 0.078 mmol) is treated with hydrazine hydrate (0.1 mL, 3.21 mmol) and p-toluenesulfonic acid monohydrate (0.01 g, 0.05 mmol) in refluxing ethanol (4 mL) for a period of 3 h. The reaction mixture is cooled to room temperature, the solid collected, washed with cold ethanol (2 x 2 mL), and air dried to give the product as a yellowish solid (0.012 g, 41.3%). mp 290-291 °C; ^{1}H NMR (DMSO-d_6) δ 8.27 (d, J = 6.8 Hz, 2H), 8.16 (d, J = 8.8 Hz, 2H), 7.42 (m, 1H), 7.12 (m, 3H), 3.81 (s, 3H), 2.90 (s, 4H), 2.70 (s, 4H), HRMS calcd. for $C_{22}H_{22}N_5O_4$ ($M+H^+$) 420.1672; found 420.1688;

EXAMPLE CLXXIV

Preparation of [3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-urea

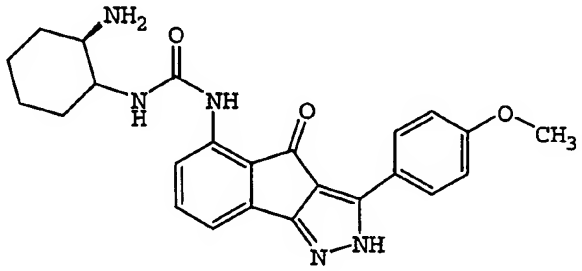


The product prepared in Example CLXXII (0.03 g, 0.072 mmol) in anhydrous DMSO (2 mL) is treated with excess ammonium hydroxide solution and 4-dimethylaminopyridine (0.005 g, 0.04 mmol) and is heated to 80 °C for 3h. The solvent is removed under reduced pressure and the residue triturated with ethanol to give a dark solid. The solid is collected and washed with ethanol (5 mL) to give urea (0.03 g, 100%). The tricarbonyl urea intermediate (0.03 g, 0.078 mmol) is treated with hydrazine hydrate (0.1 mL, 3.21 mmol) and p-toluenesulfonic acid monohydrate (0.01 g, 0.05 mmol) in refluxing ethanol (4 mL) for a period of 3 h. The

reaction mixture is cooled to room temperature, the solid collected, washed with cold ethanol (2 x 2 mL), and air dried to give the product as a yellowish solid (0.018 g, 62.4%). mp 267-269 °C; ^{1}H NMR (DMSO-d_6) δ 9.35 (s, 1H), 8.22 (m, 3H), 7.38 (m, 1H), 7.10 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 7 Hz, 1H), 3.81 (s, 3H); HRMS calcd. for $C_{18}H_{15}N_4O_3$ ($M+H^+$) 335.1144; found 335.1162;

EXAMPLE CLXXV

Preparation of 1-(2-amino-cyclohexyl)-3-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-urea

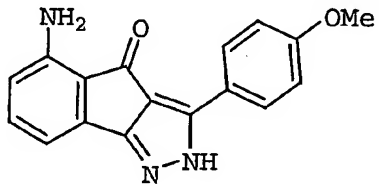


The product prepared in Example CLXXII (0.03 g, 0.072 mmol) in anhydrous DMSO (2 mL) is treated with 1,2-diaminocyclohexane (0.01g, 0.082 mmol) and 4-dimethylaminopyridine (0.005 g, 0.04 mmol) and heated to 80 °C for 3h. The solvent is removed under reduced pressure and the residue triturated with ethanol to give a dark solid. The solid is collected and washed with ethanol (5 mL) to give a tricarbonyl urea (0.03 g, 100%). The tricarbonyl urea intermediate (0.03 g, 0.078 mmol) is treated with hydrazine hydrate (0.1 mL, 3.21 mmol) and p-toluenesulfonic acid monohydrate (0.01 g, 0.05 mmol) in refluxing ethanol (4 mL) for a period of 3 h. The reaction mixture is cooled to room temperature, the solid collected, washed with cold ethanol

(2 x 2 mL), and air dried to give the product as a yellowish solid (0.01 g, 30.6%). ^{1}HNMR (DMSO-d_6) δ 9.56 (s, 1H), 8.27 (d, 1H), 8.19 (d, 2H), 7.41 (t, 1H), 7.10 (m, 3H), 4.10 (s, 1H), 3.81 (s, 3H), 3.23 (s, 1H), 1.63 (m, 5H), 1.40 (m, 3H).

EXAMPLE CLXXVI

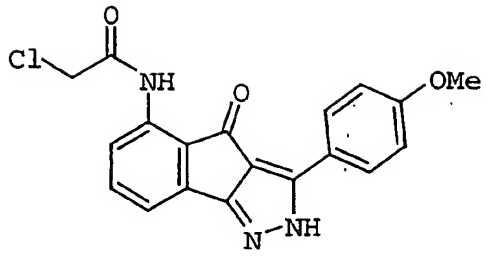
Preparation of 5-Amino-3- (4-methoxyphenyl)-2-phenyl-2H-indeno- [1,2-c]pyrazol-4-one:



A suspension of N-[3-(4-Methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-acetamide (as produced according to Nugiel, D.A.; Etzkorn, A.M.; Vidwans, A.; Benfield, P.A.; Boisclair, M.; Burton, C.R.; Cox, S.; Czerniak, P.M.; Doleniak, D.; Seitz, S.P. J. Med. Chem. 2001, 44, 1334-1336) (1.0 g, 3.0 mmol) in MeOH (10 mL) was treated with concentrated HCl (1 mL) and heated to reflux. After stirring the mixture for 2 h the reaction was cooled and the product was collected by filtration and obtained as a greenish solid (0.7 g, 81%). mp 273 °C; NMR (DMSO-d_6) δ 13.6 (bs, 1 H), 8.3 (d, J= 8.4 Hz, 1 H), 8.1 (d, J = 8.8 Hz, 2 H), 7.5 (t, J = 7.7 Hz 1 H), 7.2 (d, J = 7.0 Hz, 1 H), 7.1 (d, J = 8.8 Hz, 2 H), 3.8 (s, 3 H); HRMS m/e calc'd for $C_{17}H_{14}N_3O_2$ (M + H): 292.1086, found: 292.1080.

EXAMPLE CLXXVII

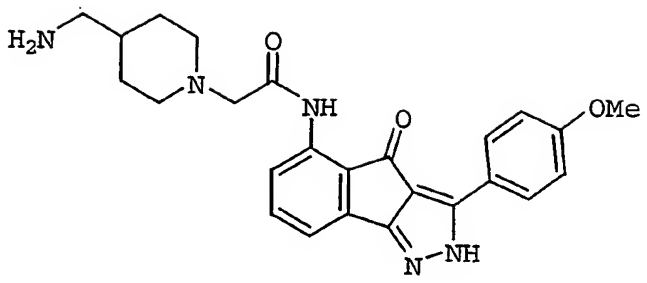
Preparation of 2-Chloro-N-[3-(4-methoxyphenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-acetamide:



A suspension of the product prepared in Example CLXXVI (0.2 g, 0.7 mmol) in dioxane (10 mL) was treated with aqueous saturated $NaHCO_3$ (3 mL) and chloroacetyl chloride (3 mL, 0.21 mmol). The reaction was heated to 50°C and stirred for 2 h. The reaction is then cooled, poured into water (20 mL), extracted with EtOAc (100 mL), the organic layer separated, dried ($MgSO_4$) and the solvent removed at reduced pressure. The residue is recrystallized from EtOH to give the product as a yellow solid (0.09 g, 35%). mp >300 °C; NMR (DMSO-d_6) δ 13.6 (bs, 1 H), 11.3 (s, 1 H), 8.3 (d, J= 8.4 Hz, 1 H), 8.1 (d, J = 8.8 Hz, 2 H), 7.5 (t, J = 7.7 Hz 1 H), 7.2 (d, J = 7.0 Hz, 1 H), 7.1 (d, J = 8.8 Hz, 2 H), 4.5 (s, 2 H), 3.8 (s, 3 H); HRMS m/e calc'd for $C_{19}H_{15}N_3O_3Cl$ (M + H): 368.0802, found: 368.0818.

EXAMPLE CLXXVIII

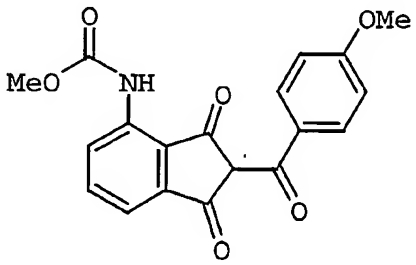
Preparation of 2-(4-aminomethyl-piperidin-1-yl)-N-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-acetamide



A suspension of product prepared according to Example CLXXVII (0.015 g, 0.04 mmol) in EtOH (1 mL) is treated with 4-aminomethylpiperdine (0.75 mL), placed in a sealed tube and heated to 80 °C for 3 h. The reaction is cooled and the solvent removed at reduced pressure. The residue is recrystallized from EtOH to give the product as a yellow solid (0.009 g, 62%).mp >300 °C; NMR (DMSO-d_6) δ 13.6 (bs, 1 H), 11.3 (s, 1 H), 8.35 (d, J= 8.4 Hz, 1 H), 8.1 (d, J = 8.8 Hz, 2 H), 7.5 (t, J = 7.7 Hz 1 H), 7.2 (d, J = 7.0 Hz, 1 H), 7.1 (d, J = 8.8 Hz, 2 H), 3.8 (s, 3 H), 3.2 (bs, 2 H), 2.9(bs, 2 H), 2.5 (d, J = 8.0 Hz, 2 H), 2.2 (t, J = 8.0 Hz, 2 H), 1.6 (m, 5 H); HRMS m/e calc'd for $C_{25}H_{28}N_5O_3$ (M + H): 446.2192, found: 446.2169; Anal. ($C_{25}H_{27}N_5O_3$) C, H, N.

EXAMPLE CLXXIX

Preparation of 2-(4-Methoxybenzoyl)-3-methoxycarbonylamino-indan-1,3-dione:

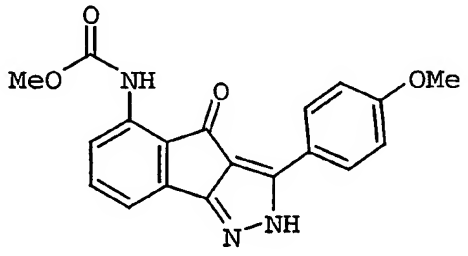


A solution of 3-methoxycarbonylamino-phthalic acid dimethyl ester (1 g, 4.8 mmol) and 4-methoxyacetophenone

(0.72 g, 4.8 mmol) in dry DMF (3 mL) was heated to 90 °C. Sodium hydride (0.21 g, 60% suspension in oil, 5.2 mmol) is added in one portion and the exothermic reaction turns deep red. After 20 min, the reaction is cooled to room temperature, diluted with water (25 mL) extracted with EtOAc (10 mL) and the aqueous phase separated. The aqueous phase is acidified to pH 2 with 2N HCl and the crude product collected. Recrystallization with ethanol gives the desired product as a yellow solid (0.4 g, 30%). ESIMS 352 (M - H, 100%).

EXAMPLE CLXXX

Preparation of 3-(4-Methoxyphenyl)-5-methoxycarbonylamino-2H-indeno-[1,2-c]pyrazol-4-one:



A solution of 2-(4-methoxybenzoyl)-3-methoxycarbonylamino-indan-1,3-dione (0.2 g, 0.6 mmol) in EtOH (5 mL) is treated with hydrazine hydrate (0.1 mL, 1.8 mmol) and p-TsOH (3 mg). The reaction is heated to reflux and stirred for 2 h. The reaction is cooled to room temperature and the product crystallized from the reaction mixture. The product is collected by filtration as a yellow solid (0.1 g, 50%). mp >300 °C; HRMS m/e calc'd for $C_{19}H_{16}N_3O_4$ (M + H): 350.1141, found: 350.1168.

UTILITY

Inhibition of Kinase/Cyclin Complex Enzymatic Activity

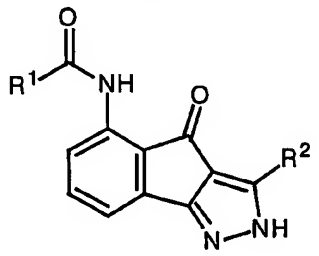
Several of the compounds disclosed in this invention were assayed for their inhibitory activity against cdk4/D1 and cdk2/E kinase complexes. Briefly, the in vitro assays employ cell lysates from insect cells expressing either of the kinases and subsequently their corresponding regulatory units. The cdk2/cyclinE is purified from insect cells expressing His-tagged cdk2 and cyclin E. The cdk/cyclin lysate is combined in a microtitre-type plate along with a kinase compatible buffer, ^{32}P-labeled ATP at a concentration of 50 mM, a GST-Rb fusion protein and the test compound at varying concentrations. The kinase reaction is allowed to proceeded with the radiolabled ATP, then effectively stopped by the addition of a large excess of EDTA and unlabeled ATP. The GST-Rb labeled protein is sequestered on a GSH-Sepharose bead suspension, washed, resuspended in scintillant, and the ^{32}P activity detected in a scintillation counter. The compound concentration which inhibits 50% of the kinase activity was calculated for each compound. A compound was considered active if its IC_{50} was found to be less than 1 μM.

Inhibition of HCT 116 Cancer Cell Proliferation

To test the cellular activity of several compounds disclosed in this invention, we examined the effect of these compounds on cultured HCT116 cells and determined their effect on cell-cycle progression by the colorimetric cytotoxcity test using sulforhodamine B (Skehan et al. J. Natl. Cancer Inst. 82:1107-12, 1990). Briefly, HCT116 cells are cultured in the presence of test compounds at increasing concentrations. At selected time points, groups of cells are fixed with trichloroacetic acid and stained with

sulforhodamine B (SRB). Unbound dye was removed by washing and protein-bound dye was extracted for determination of optical density. A compound was considered active if its IC_{50} was found to be less than 10 μM.

Table 1



Example #	R^1	R^2	mass (M^+H)	mp (°C)
I	Methyl	4-$MeOC_6H_4$	334	268
II	$ClCH_2$	4-$MeOC_6H_4$	382	274
III	Cyclopropyl	4-$MeOC_6H_4$	360	289
IV	Isopropyl	4-$MeOC_6H_4$	362	288
V	Ethyl	4-$MeOC_6H_4$	348	287
VI	Cyclopentyl	4-$MeOC_6H_4$	388	267
VII	Cyclobutyl	4-$MeOC_6H_4$	374	297
VIII	Benzyl	4-$MeOC_6H_4$	410	280
IX	n-propyl	4-$MeOC_6H_4$	362	282
X	4-$ClC_6H_4CH_2$	4-$MeOC_6H_4$	444	238
XI	3-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$	440	>300
XII	4-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$	440	280
XIII	3,4-di$MeOC_6H_4CH_2$	4-$MeOC_6H_4$	470	>300
XIV	2,5-di$MeOC_6H_4CH_2$	4-$MeOC_6H_4$	470	226

XV	Methyl	2-$MeOC_6H_4$	334	276
XVI	Methyl	3,4-di$MeOC_6H_4$	364	>300
XVII	3,4-$(OCH_2O)C_6H_4CH_2$	4-$MeOC_6H_4$	454	297
XVIII	3-thiophenylCH_2	4-$MeOC_6H_4$	416	293
XIX	2-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$	440	255
XX	3,4-di$ClOC_6H_4CH_2$	4-$MeOC_6H_4$	479	299
XXI	2,4-di$ClOC_6H_4CH_2$	4-$MeOC_6H_4$	479	286
XXII	2-$ClC_6H_4CH_2$	4-$MeOC_6H_4$	444	300
XXIII	H_2NCH_2	4-$MeOC_6H_4$	349	>300
XXIV	$HOCH_2CH_2NHCH_2$	4-$MeOC_6H_4$	393	243
XXV	Me_2NCH_2	4-$MeOC_6H_4$	377	279
XXVI	piperazinylCH_2	4-$MeOC_6H_4$	418	277
XXVII	4-Me-piperazinylCH_2	4-$MeOC_6H_4$	432	>300
XXVIII	4-$HOCH_2CH_2$-piperazinylCH_2	4-$MeOC_6H_4$	462	>300
XXIX	piperidinylCH_2	4-$MeOC_6H_4$	417	291
XXX	4-NH_2CH_2-piperidinylCH_2	4-$MeOC_6H_4$	446	>300
XXXI	$CH_3CH_2NHCH_2$	4-$MeOC_6H_4$	377	250
XXXII	ThiomorpholinylCH_2	4-$MeOC_6H_4$	435	298
XXXIII	morpholinylCH_2	4-$MeOC_6H_4$	419	295
XXXIV	pyrrolidinylCH_2	4-$MeOC_6H_4$	403	279
XXXV	4-pyridylCH_2NHCH_2	4-$MeOC_6H_4$	440	>300
XXXVI	4-$CH_3CONHC_6H_4CH_2$	4-$MeOC_6H_4$	467	268
XXXVII	4-$CH_3OCONHC_6H_4CH_2$	4-$MeOC_6H_4$	483	257
XXXVIII	4-$NH_2CH_2CONHC_6H_4CH_2$	4-$MeOC_6H_4$	482	228
XXXIX	4-$Me_2NCH_2CONHC_6H_4CH_2$	4-$MeOC_6H_4$	510	>300
XL	4-$N_3C_6H_4CH_2$	4-$MeOC_6H_4$	451	>300

XLI	4-$NH_2C_6H_4CH_2$	4-$MeOC_6H_4$	425	283
XLII	C_6H_5NH	4-$MeOC_6H_4$	411	>300
XLIII	$CH_3CH_2CH_2NH$	4-$MeOC_6H_4$	377	252
XLIV	4-$NH_2C_6H_4CH_2NH$	4-$MeOC_6H_4$	440	>300
XLV	4-pyridylCH_2NH	4-$MeOC_6H_4$	426	>300
XLVI	Methyl	4-HOC_6H_4	320	>300
XLVII	H	4-$MeOC_6H_4$	320	280
XLVIII	Methyl	3-pyridyl	305	>300
XLIX	Methyl	4-pyridyl	305	>300
L	H	4-pyridyl	291	>300
LI	Methyl	C_6H_5	305	>300
LII	Methyl	4-$MeSC_6H_4$	351	283
LIII	Methyl	4-$MeSO_2C_6H_4$	383	>300
LVI	Methyl	4-$Me_2NC_6H_4$	348	>300
LV	morpholinylCH_2	4-$Me_2NC_6H_4$	432	>300
LVI	Me_2NCH_2	4-$Me_2NC_6H_4$	390	>300
LVII	Methyl	4-(piperdinyl)C_6H_4	388	291
LVIII	Methyl	4-(morpholinyl)C_6H_4	389	>300
LIX	Methyl	4-$CH_3CH_2OC_6H_4$	349	288
LX	Methyl	4-$CH_3CH_2CH_2CH_2C_6H_4$	361	259
LXI	Methyl	4-$CH_3CH_2C_6H_4$	332	294
LXII	Methyl	4-$CH_3CH_2CH_2C_6H_4$	347	269
LXIII	NH_2	4-$MeOC_6H_4$	335	>300
LXIV	Me2NNH	4-$MeOC_6H_4$	378	>300
LXV	MeNH	4-$MeOC_6H_4$	349	>300
LXVI	MorpholinylNH	4-$MeOC_6H_4$	420	>300

LXVII	cis-1,2-diaminocyclohexanyl	4-$MeOC_6H_4$	432	>300
LXVIII	4-methylpiperazinylNH	4-$MeOC_6H_4$	433	>300
LXVIX	4-uridomethylpiperadinylCH_2	4-$MeOC_6H_4$	489	>300
LXX	4-(2-pyridyl)piperazinyl CH_2	4-$MeOC_6H_4$	495	>300
LXXI	4-(aminoethyl)piperazinyl CH_2	4-$MeOC_6H_4$	461	>300
LXXII	4-amidopiperidinylCH_2	4-$MeOC_6H_4$	460	>300
LXXIII	4-hydroxypiperidinylCH_2	4-$MeOC_6H_4$	433	>300
LXXIV	4-hydroxymethylpiperidinylCH_2	4-$MeOC_6H_4$	447	>300
LXXV	4-amidopiperazinylCH_2	4-$MeOC_6H_4$	493	>300
LXXVI	4-dimethylaminopiperadinylCH_2	4-$MeOC_6H_4$	492	>300
LXXVII	4-aminopiperadinylCH_2	4-$MeOC_6H_4$	464	>300
LXXVIII	4-Me-piperazinylCH2	4-$Me_2NC_6H_4$	445	>300
LXXIX	4-NH_2CH_2-piperidinylCH2	4-$Me_2NC_6H_4$	459	NA
LXXX	4-OH-piperidinylCH2	4-$Me_2NC_6H_4$	446	267
LXXXI	morpholinylCH_2	4-(morpholinyl)C_6H_4	474	258

LXXXII	4-Me-piperazinylCH_2	4-(morpholinyl)C_6H_4	487	258
LXXXIII	4-OH-piperidinylCH_2	4-(morpholinyl)C_6H_4	488	245
LXXXIV	4-NH_2CH_2-piperidinylCH_2	4-(morpholinyl)C_6H_4	501	240
LXXXV	4-Me-piperazinylNH	4-$Me_2NC_6H_4$	446	>300
LXXXVI	Methyl	i-propyl	270	>250
LXXXVII	Methyl	c-propyl	268	220
LXXXVIII	Methyl	t-butyl	284	>250
LXXXIX	Methyl	2-thienyl	310	269
XC	Methyl	3-Me-2-thienyl	324	275
XCI	NH_2	Ethyl	257	>250
XCII	NH_2	n-propyl	271	187
XCIII	NH_2	i-propyl	271	>250
XCIV	NH_2	c-propyl	267 (M-H)	252
XCV	NH_2	c-hexyl	311	178
XCVI	NH_2	2-thienyl	310 (M+)	214
XCVII	NH_2	3-Me-2-thienyl	325	270
XCVIII	NH_2	5-Me-2-thienyl	325	>280
XCIX	NH_2	5-CO_2Et-2-thienyl	383	>280
C	NH_2	3-thienyl	311	>280
CI	NH_2	5-Cl-3-thienyl	345	>300
CII	NH_2	2,5-diMe-3-thienyl	339	>280
CIII	NH_2	2-furanyl	295	278
CIV	Me_2NNH	i-propyl	314	231
CV	Me_2NNH	c-propyl	312	
CVI	Me_2NNH	c-hexyl	354	229

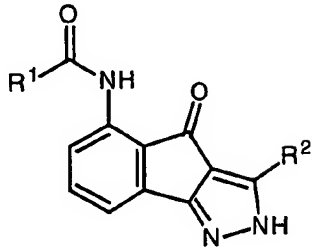
CVII	Me_2NNH	2-thienyl	354	279
CVIII	Me_2NNH	5-MeO-2-thienyl	384	>280
CIX	Me_2NNH	5-Me-2-thienyl	368	>280
CX	Me_2NNH	5-CO_2Et-2-thienyl	426	252
CXI	Me_2NNH	3-thienyl	354	202
CXII	NH_2	1-methyl-3-pyrrolyl	308	>300
CXIII	Me_2NNH	2,5-diMe-3-thienyl	382	252
CXIV	Me_2NNH	2-furanyl	338	202
CXV	4-NH_2CO-piperidinylCH_2	i-propyl	396	224
CXVI	4-NH_2CO-piperidinylCH_2	c-hexyl	436	228
CXVII	4-NH_2CH_2-piperidinylCH_2	ethyl	368	174
CXVIII	4-NH_2CH_2-piperidinylCH_2	i-propyl	382	218
CXVIX	4-NH_2CH_2-piperidinylCH_2	c-propyl	380	138
CXX	4-NH_2CH_2-piperidinylCH_2	c-hexyl	422	196
CXXI	4-CH_3-piperazinylNH	i-propyl	369	231
CXXII	4-CH_3-piperazinylNH	5-CO_2Et-2-thienyl	481	249
CXXIII	4-CH_3-piperazinylNH	5-CO_2H-2-thienyl	453	270
CXXIV	4-CH_3-piperazinylNH	2,5-diMe-3-thienyl	437	250
CXXV	MorpholinylNH	i-propyl	354 (M-H)	256
CXXVI	MorpholinylNH	4-CO_2Me-piperidinyl	455	216
CXXVII	MorpholinylNH	5-Me-2-thienyl	410	261

CXXVIII	MorpholinylNH	5-Cl-3-thienyl	430	259
CXXIX	MorpholinylNH	2,5-diMe-3-thienyl	424	>280
CXXX	MorpholinylNH	5-CO_2Et-2-thienyl	468	258
CXXXI	MorpholinylNH	5-CO_2H-2-thienyl	440	273
CXXXII	MorpholinylNH	5-CONHBn-2-thienyl	529	275
CXXXIII	MorpholinylNH	5-CONH(4-Me-piperazinyl)-2-thienyl	537	190
CXXXIV	MorpholinylNH	5-CONHCH$_2$CH$_2$(1-Me-2-pyrrolidinyl)-2-thienyl	550	235
CXXXV	MorpholinylNH	5-CONHNMe$_2$-2-thienyl	482	201
CXXXVI	MorpholinylNH	5-CONHCH$_2$CH$_2$NMe$_2$-2-thienyl	510	190
CXXXVII	MorpholinylNH	5-CONHCH$_2$CH$_2$(1-pyrrolidinyl)-2-thienyl	536	224
CXXXVIII	MorpholinylNH	5-CONHCH$_2$CH$_2$(1-morpholinyl)-2-thienyl	552	241
CXXXIX	MorpholinylNH	5-CONHmorpholinyl-2-thienyl	524	271
CXL	MorpholinylNH	5-CONHCH$_2$CH$_2$CH$_2$(1-pyrrolidonyl)-2-thienyl	564	260
CXLI	MorpholinylNH	5-CONHCH$_2$CH$_2$(3-pyridyl)-2-thienyl	544	203
CXLII	MorpholinylNH	5-CONHCH$_2$CH$_2$CH$_2$(1-imidazolyl)-2-thienyl	547	263

CXLIII	MorpholinylNH	5-$CONHCH_2CH_2$(2-pyridyl)-2-thienyl	544	>280
CXLIV	MorpholinylNH	5-$CONHCH_2$(3-pyridyl)-2-thienyl	530	239
CXLV	MorpholinylNH	5-$CONHCH_2CH_2$(1-piperidinyl)-2-thienyl	550	228
CXLVI	Methyl	4-$CF_3C_6H_4$	370 $(M-H)^-$	>300
CXLVII	MorpholinylNH	4-(4-Boc-piperazinyl)C_6H_4	574	242
CXLVIII	MorpholinylNH	4-(piperazinyl)C_6H_4	474	263
CXLIX	NH_2	4-(piperazinyl)C_6H_4	389	257
CL	NH_2NH	4-(piperazinyl)C_6H_4	404	257
CLI	Me_2NCH_2	4-(piperazinyl)C_6H_4	431	243
CLII	morpholinylCH_2	4-(piperazinyl)C_6H_4	473	259
CLIII	4-Me-piperazinylCH_2	4-(piperazinyl)C_6H_4	486	NA
CLIV	4-NH_2CH_2-piperidinylCH_2	4-(piperazinyl)C_6H_4	500	239
CLV	MorpholinylNH	4-(4-Me-piperazinyl)C_6H_4	488	245
CLVI	MorpholinylNH	4-(4-Et-piperazinyl)C_6H_4	502	245

CLVII	MorpholinylNH	4-(4-i-Pr-piperazinyl)C_6H_4	516	253
CLVIII	$C_6H_5C(O)NHNH$	4-$MeOC_6H_4$	459	>300
CLIX	4-pyridylC(O)NHNH	4-$MeOC_6H_4$	455	248
CLX	3-pyridylC(O)NHNH	4-$MeOC_6H_4$	455	227
CLXI	3,4-dihydroxy-$C_6H_3C(O)NHNH$	4-$MeOC_6H_4$	486	>300
CLXII	4-hydroxy-$C_6H_4C(O)NHNH$	4-$MeOC_6H_4$	470	283
CLXIII	3-amino-$C_6H_4C(O)NHNH$	4-$MeOC_6H_4$	469	250
CLXIV	4-amino-$C_6H_4C(O)NHNH$	4-$MeOC_6H_4$	469	247
CLXV	2-amino-$C_6H_4C(O)NHNH$	4-$MeOC_6H_4$	469	257
CLXVI	4-N,N-dimethylamino-$C_6H_4C(O)NHNH$	4-$MeOC_6H_4$	497	259
CLXVII	$C_6H_5CH_2C(O)NHNH$	4-$MeOC_6H_4$	468	269
CLXVIII	2-hydroxy-$C_6H_4C(O)NHNH$	4-$MeOC_6H_4$	470	280
CLXIX	$MeOC(O)NHNH$	4-$MeOC_6H_4$	408	>300

Table 2



Example Number	R^1	R^2
100	2-pyridylmethyl	4-$MeOC_6H_4$

	101	2-pyridylmethyl	3-$MeOC_6H_4$
	102	2-pyridylmethyl	4-$NH_2C_6H_4$
	103	2-pyridylmethyl	3-$NH_2C_6H_4$
	104	2-pyridylmethyl	2-$NH_2C_6H_4$
	105	2-pyridylmethyl	4-$Me_2NC_6H_4$
	106	2-pyridylmethyl	3-$Me_2NC_6H_4$
	107	2-pyridylmethyl	2-$Me_2NC_6H_4$
	108	2-pyridylmethyl	4-pyridyl
	109	2-pyridylmethyl	3-pyridyl
	110	2-pyridylmethyl	2-pyridyl
	111	2-pyridylmethyl	2-thiazolyl
	112	2-pyridylmethyl	2-pyrazolyl
	113	2-pyridylmethyl	5-isoquinolyl
	114	2-pyridylmethyl	3,4-methylenedioxyC_6H_3
	115	2-pyridylmethyl	3,4-ethylenedioxyC_6H_3
	116	2-pyridylmethyl	2-imidazolyl
	117	2-pyridylmethyl	2-oxazolyl
	118	2-pyridylmethyl	4-isoxazolyl
	119	2-pyridylmethyl	4-HOC_6H_4
	120	2-pyridylmethyl	3-HOC_6H_4
	121	2-pyridylmethyl	3,4-diHOC_6H_4
	122	2-pyridylmethyl	4-$NH_2CH_2C_6H_4$
	123	2-pyridylmethyl	3-$NH_2CH_2C_6H_4$
	124	3-pyridylmethyl	4-$MeOC_6H_4$
	125	3-pyridylmethyl	3-$MeOC_6H_4$
	126	3-pyridylmethyl	4-$NH_2C_6H_4$
	127	3-pyridylmethyl	3-$NH_2C_6H_4$
	128	3-pyridylmethyl	2-$NH_2C_6H_4$

129	3-pyridylmethyl	4-$Me_2NC_6H_4$
130	3-pyridylmethyl	3-$Me_2NC_6H_4$
131	3-pyridylmethyl	2-$Me_2NC_6H_4$
132	3-pyridylmethyl	4-pyridyl
133	3-pyridylmethyl	3-pyridyl
134	3-pyridylmethyl	2-pyridyl
135	3-pyridylmethyl	2-thiazolyl
136	3-pyridylmethyl	2-pyrazolyl
137	3-pyridylmethyl	5-isoquinolyl
138	3-pyridylmethyl	3,4-methylenedioxyC_6H_3
139	3-pyridylmethyl	3,4-ethylenedioxyC_6H_3
140	3-pyridylmethyl	2-imidazolyl
141	3-pyridylmethyl	2-oxazolyl
142	3-pyridylmethyl	4-isoxazolyl
143	3-pyridylmethyl	4-HOC_6H_4
144	3-pyridylmethyl	3-HOC_6H_4
145	3-pyridylmethyl	3,4-diHOC_6H_4
146	3-pyridylmethyl	4-$NH_2CH_2C_6H_4$
147	3-pyridylmethyl	3-$NH_2CH_2C_6H_4$
148	4-pyridylmethyl	4-$MeOC_6H_4$
149	4-pyridylmethyl	3-$MeOC_6H_4$
150	4-pyridylmethyl	4-$NH_2C_6H_4$
151	4-pyridylmethyl	3-$NH_2C_6H_4$
152	4-pyridylmethyl	2-$NH_2C_6H_4$
153	4-pyridylmethyl	4-$Me_2NC_6H_4$
154	4-pyridylmethyl	3-$Me_2NC_6H_4$
155	4-pyridylmethyl	2-$Me_2NC_6H_4$
156	4-pyridylmethyl	4-pyridyl

	157	4-pyridylmethyl	3-pyridyl
	158	4-pyridylmethyl	2-pyridyl
	159	4-pyridylmethyl	2-thiazolyl
	160	4-pyridylmethyl	2-pyrazolyl
	161	4-pyridylmethyl	5-isoquinolyl
	162	4-pyridylmethyl	3,4-methylenedioxyC_6H_3
	163	4-pyridylmethyl	3,4-ethylenedioxyC_6H_3
	164	4-pyridylmethyl	2-imidazolyl
	165	4-pyridylmethyl	2-oxazolyl
	166	4-pyridylmethyl	4-isoxazolyl
	167	4-pyridylmethyl	4-HOC_6H_4
	168	4-pyridylmethyl	3-HOC_6H_4
	169	4-pyridylmethyl	3,4-diHOC_6H_4
	170	4-pyridylmethyl	4-$NH_2CH_2C_6H_4$
	171	4-pyridylmethyl	3-$NH_2CH_2C_6H_4$
	172	2-$NH_2C_6H_4CH_2$	4-$MeOC_6H_4$
	173	2-$NH_2C_6H_4CH_2$	3-$MeOC_6H_4$
	174	2-$NH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
	175	2-$NH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
	176	2-$NH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
	177	2-$NH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	178	2-$NH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	179	2-$NH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	180	2-$NH_2C_6H_4CH_2$	4-pyridyl
	181	2-$NH_2C_6H_4CH_2$	3-pyridyl
	182	2-$NH_2C_6H_4CH_2$	2-pyridyl
	183	2-$NH_2C_6H_4CH_2$	2-thiazolyl
	184	2-$NH_2C_6H_4CH_2$	2-pyrazolyl

185	2-$NH_2C_6H_4CH_2$	5-isoquinolyl
186	2-$NH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
187	2-$NH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
188	2-$NH_2C_6H_4CH_2$	2-imidazolyl
189	2-$NH_2C_6H_4CH_2$	2-oxazolyl
190	2-$NH_2C_6H_4CH_2$	4-isoxazolyl
191	2-$NH_2C_6H_4CH_2$	4-HOC_6H_4
192	2-$NH_2C_6H_4CH_2$	3-HOC_6H_4
193	2-$NH_2C_6H_4CH_2$	3,4-diHOC_6H_4
194	2-$NH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
195	2-$NH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
196	3-$NH_2C_6H_4CH_2$	3-$MeOC_6H_4$
197	3-$NH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
198	3-$NH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
199	3-$NH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
200	3-$NH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
201	3-$NH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
202	3-$NH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
203	3-$NH_2C_6H_4CH_2$	4-pyridyl
204	3-$NH_2C_6H_4CH_2$	3-pyridyl
205	3-$NH_2C_6H_4CH_2$	2-pyridyl
206	3-$NH_2C_6H_4CH_2$	2-thiazolyl
207	3-$NH_2C_6H_4CH_2$	2-pyrazolyl
208	3-$NH_2C_6H_4CH_2$	5-isoquinolyl
209	3-$NH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3

	210	3-$NH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	211	3-$NH_2C_6H_4CH_2$	2-imidazolyl
	212	3-$NH_2C_6H_4CH_2$	2-oxazolyl
	213	3-$NH_2C_6H_4CH_2$	4-isoxazolyl
	214	3-$NH_2C_6H_4CH_2$	4-HOC_6H_4
	215	3-$NH_2C_6H_4CH_2$	3-HOC_6H_4
	216	3-$NH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	217	3-$NH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	218	3-$NH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	219	4-$NH_2C_6H_4CH_2$	3-$MeOC_6H_4$
	220	4-$NH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
	221	4-$NH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
	222	4-$NH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
	223	4-$NH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	224	4-$NH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	225	4-$NH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	226	4-$NH_2C_6H_4CH_2$	4-pyridyl
	227	4-$NH_2C_6H_4CH_2$	3-pyridyl
	228	4-$NH_2C_6H_4CH_2$	2-pyridyl
	229	4-$NH_2C_6H_4CH_2$	2-thiazolyl
	230	4-$NH_2C_6H_4CH_2$	2-pyrazolyl
	231	4-$NH_2C_6H_4CH_2$	5-isoquinolyl
	232	4-$NH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	233	4-$NH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	234	4-$NH_2C_6H_4CH_2$	2-imidazolyl
	235	4-$NH_2C_6H_4CH_2$	2-oxazolyl

	236	4-$NH_2C_6H_4CH_2$	4-isoxazolyl
	237	4-$NH_2C_6H_4CH_2$	4-HOC_6H_4
	238	4-$NH_2C_6H_4CH_2$	3-HOC_6H_4
	239	4-$NH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	240	4-$NH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	241	4-$NH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	242	2-$MeOC_6H_4CH_2$	3-$MeOC_6H_4$
	243	2-$MeOC_6H_4CH_2$	4-$NH_2C_6H_4$
	244	2-$MeOC_6H_4CH_2$	3-$NH_2C_6H_4$
	245	2-$MeOC_6H_4CH_2$	2-$NH_2C_6H_4$
	246	2-$MeOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	247	2-$MeOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	248	2-$MeOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	249	2-$MeOC_6H_4CH_2$	4-pyridyl
	250	2-$MeOC_6H_4CH_2$	3-pyridyl
	251	2-$MeOC_6H_4CH_2$	2-pyridyl
	252	2-$MeOC_6H_4CH_2$	2-thiazolyl
	253	2-$MeOC_6H_4CH_2$	2-pyrazolyl
	254	2-$MeOC_6H_4CH_2$	5-isoquinolyl
	255	2-$MeOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	256	2-$MeOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	257	2-$MeOC_6H_4CH_2$	2-imidazolyl
	258	2-$MeOC_6H_4CH_2$	2-oxazolyl
	259	2-$MeOC_6H_4CH_2$	4-isoxazolyl
	260	2-$MeOC_6H_4CH_2$	4-HOC_6H_4
	261	2-$MeOC_6H_4CH_2$	3-HOC_6H_4
	262	2-$MeOC_6H_4CH_2$	3,4-diHOC_6H_4

263	2-$MeOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
264	2-$MeOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
265	3-$MeOC_6H_4CH_2$	3-$MeOC_6H_4$
266	3-$MeOC_6H_4CH_2$	4-$NH_2C_6H_4$
267	3-$MeOC_6H_4CH_2$	3-$NH_2C_6H_4$
268	3-$MeOC_6H_4CH_2$	2-$NH_2C_6H_4$
269	3-$MeOC_6H_4CH_2$	4-$Me_2NC_6H_4$
270	3-$MeOC_6H_4CH_2$	3-$Me_2NC_6H_4$
271	3-$MeOC_6H_4CH_2$	2-$Me_2NC_6H_4$
272	3-$MeOC_6H_4CH_2$	4-pyridyl
273	3-$MeOC_6H_4CH_2$	3-pyridyl
274	3-$MeOC_6H_4CH_2$	2-pyridyl
275	3-$MeOC_6H_4CH_2$	2-thiazolyl
276	3-$MeOC_6H_4CH_2$	2-pyrazolyl
277	3-$MeOC_6H_4CH_2$	5-isoquinolyl
278	3-$MeOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
279	3-$MeOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
280	3-$MeOC_6H_4CH_2$	2-imidazolyl
281	3-$MeOC_6H_4CH_2$	2-oxazolyl
282	3-$MeOC_6H_4CH_2$	4-isoxazolyl
283	3-$MeOC_6H_4CH_2$	4-HOC_6H_4
284	3-$MeOC_6H_4CH_2$	3-HOC_6H_4
285	3-$MeOC_6H_4CH_2$	3,4-diHOC_6H_4
286	3-$MeOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
287	3-$MeOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
288	4-$MeOC_6H_4CH_2$	3-$MeOC_6H_4$
289	4-$MeOC_6H_4CH_2$	4-$NH_2C_6H_4$

	290	4-$MeOC_6H_4CH_2$	3-$NH_2C_6H_4$
	291	4-$MeOC_6H_4CH_2$	2-$NH_2C_6H_4$
	292	4-$MeOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	293	4-$MeOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	294	4-$MeOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	295	4-$MeOC_6H_4CH_2$	4-pyridyl
	296	4-$MeOC_6H_4CH_2$	3-pyridyl
	297	4-$MeOC_6H_4CH_2$	2-pyridyl
	298	4-$MeOC_6H_4CH_2$	2-thiazolyl
	299	4-$MeOC_6H_4CH_2$	2-pyrazolyl
	300	4-$MeOC_6H_4CH_2$	5-isoquinolyl
	301	4-$MeOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	302	4-$MeOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	303	4-$MeOC_6H_4CH_2$	2-imidazolyl
	304	4-$MeOC_6H_4CH_2$	2-oxazolyl
	305	4-$MeOC_6H_4CH_2$	4-isoxazolyl
	306	4-$MeOC_6H_4CH_2$	4-HOC_6H_4
	307	4-$MeOC_6H_4CH_2$	3-HOC_6H_4
	308	4-$MeOC_6H_4CH_2$	3,4-diHOC_6H_4
	309	4-$MeOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	310	4-$MeOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	311	2-$HOC_6H_4CH_2$	4-$MeOC_6H_4$
	312	2-$HOC_6H_4CH_2$	3-$MeOC_6H_4$
	313	2-$HOC_6H_4CH_2$	4-$NH_2C_6H_4$
	314	2-$HOC_6H_4CH_2$	3-$NH_2C_6H_4$
	315	2-$HOC_6H_4CH_2$	2-$NH_2C_6H_4$
	316	2-$HOC_6H_4CH_2$	4-$Me_2NC_6H_4$

317	2-$HOC_6H_4CH_2$	3-$Me_2NC_6H_4$
318	2-$HOC_6H_4CH_2$	2-$Me_2NC_6H_4$
319	2-$HOC_6H_4CH_2$	4-pyridyl
320	2-$HOC_6H_4CH_2$	3-pyridyl
321	2-$HOC_6H_4CH_2$	2-pyridyl
322	2-$HOC_6H_4CH_2$	2-thiazolyl
323	2-$HOC_6H_4CH_2$	2-pyrazolyl
324	2-$HOC_6H_4CH_2$	5-isoquinolyl
325	2-$HOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
326	2-$HOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
327	2-$HOC_6H_4CH_2$	2-imidazolyl
328	2-$HOC_6H_4CH_2$	2-oxazolyl
329	2-$HOC_6H_4CH_2$	4-isoxazolyl
330	2-$HOC_6H_4CH_2$	4-HOC_6H_4
331	2-$HOC_6H_4CH_2$	3-HOC_6H_4
332	2-$HOC_6H_4CH_2$	3,4-diHOC_6H_4
333	2-$HOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
334	2-$HOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
335	3-$HOC_6H_4CH_2$	4-$MeOC_6H_4$
336	3-$HOC_6H_4CH_2$	3-$MeOC_6H_4$
337	3-$HOC_6H_4CH_2$	4-$NH_2C_6H_4$
338	3-$HOC_6H_4CH_2$	3-$NH_2C_6H_4$
339	3-$HOC_6H_4CH_2$	2-$NH_2C_6H_4$
340	3-$HOC_6H_4CH_2$	4-$Me_2NC_6H_4$
341	3-$HOC_6H_4CH_2$	3-$Me_2NC_6H_4$
342	3-$HOC_6H_4CH_2$	2-$Me_2NC_6H_4$
343	3-$HOC_6H_4CH_2$	4-pyridyl

	344	3-$HOC_6H_4CH_2$	3-pyridyl
	345	3-$HOC_6H_4CH_2$	2-pyridyl
	346	3-$HOC_6H_4CH_2$	2-thiazolyl
	347	3-$HOC_6H_4CH_2$	2-pyrazolyl
	348	3-$HOC_6H_4CH_2$	5-isoquinolyl
	349	3-$HOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	350	3-$HOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	351	3-$HOC_6H_4CH_2$	2-imidazolyl
	352	3-$HOC_6H_4CH_2$	2-oxazolyl
	353	3-$HOC_6H_4CH_2$	4-isoxazolyl
	354	3-$HOC_6H_4CH_2$	4-HOC_6H_4
	355	3-$HOC_6H_4CH_2$	3-HOC_6H_4
	356	3-$HOC_6H_4CH_2$	3,4-diHOC_6H_4
	357	3-$HOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	358	3-$HOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	359	4-$HOC_6H_4CH_2$	4-$MeOC_6H_4$
	360	4-$HOC_6H_4CH_2$	3-$MeOC_6H_4$
	361	4-$HOC_6H_4CH_2$	4-$NH_2C_6H_4$
	362	4-$HOC_6H_4CH_2$	3-$NH_2C_6H_4$
	363	4-$HOC_6H_4CH_2$	2-$NH_2C_6H_4$
	364	4-$HOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	365	4-$HOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	366	4-$HOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	367	4-$HOC_6H_4CH_2$	4-pyridyl
	368	4-$HOC_6H_4CH_2$	3-pyridyl
	369	4-$HOC_6H_4CH_2$	2-pyridyl
	370	4-$HOC_6H_4CH_2$	2-thiazolyl

371	4-$HOC_6H_4CH_2$	2-pyrazolyl
372	4-$HOC_6H_4CH_2$	5-isoquinolyl
373	4-$HOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
374	4-$HOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
375	4-$HOC_6H_4CH_2$	2-imidazolyl
376	4-$HOC_6H_4CH_2$	2-oxazolyl
377	4-$HOC_6H_4CH_2$	4-isoxazolyl
378	4-$HOC_6H_4CH_2$	4-HOC_6H_4
379	4-$HOC_6H_4CH_2$	3-HOC_6H_4
380	4-$HOC_6H_4CH_2$	3,4-diHOC_6H_4
381	4-$HOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
382	4-$HOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
383	4-$ClC_6H_4CH_2$	3-$MeOC_6H_4$
384	4-$ClC_6H_4CH_2$	4-$NH_2C_6H_4$
385	4-$ClC_6H_4CH_2$	3-$NH_2C_6H_4$
386	4-$ClC_6H_4CH_2$	2-$NH_2C_6H_4$
387	4-$ClC_6H_4CH_2$	4-$Me_2NC_6H_4$
388	4-$ClC_6H_4CH_2$	3-$Me_2NC_6H_4$
389	4-$ClC_6H_4CH_2$	2-$Me_2NC_6H_4$
390	4-$ClC_6H_4CH_2$	4-pyridyl
391	4-$ClC_6H_4CH_2$	3-pyridyl
392	4-$ClC_6H_4CH_2$	2-pyridyl
393	4-$ClC_6H_4CH_2$	2-thiazolyl
394	4-$ClC_6H_4CH_2$	2-pyrazolyl
395	4-$ClC_6H_4CH_2$	5-isoquinolyl
396	4-$ClC_6H_4CH_2$	3,4-methylenedioxyC_6H_3

	397	4-$ClC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	398	4-$ClC_6H_4CH_2$	2-imidazolyl
	399	4-$ClC_6H_4CH_2$	2-oxazolyl
	400	4-$ClC_6H_4CH_2$	4-isoxazolyl
	401	4-$ClC_6H_4CH_2$	4-HOC_6H_4
	402	4-$ClC_6H_4CH_2$	3-HOC_6H_4
	403	4-$ClC_6H_4CH_2$	3,4-diHOC_6H_4
	404	4-$ClC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	405	4-$ClC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	406	2-$NH_2CH_2C_6H_4CH_2$	4-$MeOC_6H_4$
	407	2-$NH_2CH_2C_6H_4CH_2$	3-$MeOC_6H_4$
	408	2-$NH_2CH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
	409	2-$NH_2CH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
	410	2-$NH_2CH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
	411	2-$NH_2CH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	412	2-$NH_2CH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	413	2-$NH_2CH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	414	2-$NH_2CH_2C_6H_4CH_2$	4-pyridyl
	415	2-$NH_2CH_2C_6H_4CH_2$	3-pyridyl
	416	2-$NH_2CH_2C_6H_4CH_2$	2-pyridyl
	417	2-$NH_2CH_2C_6H_4CH_2$	2-thiazolyl
	418	2-$NH_2CH_2C_6H_4CH_2$	2-pyrazolyl
	419	2-$NH_2CH_2C_6H_4CH_2$	5-isoquinolyl
	420	2-$NH_2CH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	421	2-$NH_2CH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	422	2-$NH_2CH_2C_6H_4CH_2$	2-imidazolyl

423	2-$NH_2CH_2C_6H_4CH_2$	2-oxazolyl
424	2-$NH_2CH_2C_6H_4CH_2$	4-isoxazolyl
425	2-$NH_2CH_2C_6H_4CH_2$	4-HOC_6H_4
426	2-$NH_2CH_2C_6H_4CH_2$	3-HOC_6H_4
427	2-$NH_2CH_2C_6H_4CH_2$	3,4-diHOC_6H_4
428	2-$NH_2CH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
429	2-$NH_2CH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
430	3-$NH_2CH_2C_6H_4CH_2$	4-$MeOC_6H_4$
431	3-$NH_2CH_2C_6H_4CH_2$	3-$MeOC_6H_4$
432	3-$NH_2CH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
433	3-$NH_2CH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
434	3-$NH_2CH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
435	3-$NH_2CH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
436	3-$NH_2CH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
437	3-$NH_2CH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
438	3-$NH_2CH_2C_6H_4CH_2$	4-pyridyl
439	3-$NH_2CH_2C_6H_4CH_2$	3-pyridyl
440	3-$NH_2CH_2C_6H_4CH_2$	2-pyridyl
441	3-$NH_2CH_2C_6H_4CH_2$	2-thiazolyl
442	3-$NH_2CH_2C_6H_4CH_2$	2-pyrazolyl
443	3-$NH_2CH_2C_6H_4CH_2$	5-isoquinolyl
444	3-$NH_2CH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
445	3-$NH_2CH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
446	3-$NH_2CH_2C_6H_4CH_2$	2-imidazolyl
447	3-$NH_2CH_2C_6H_4CH_2$	2-oxazolyl
448	3-$NH_2CH_2C_6H_4CH_2$	4-isoxazolyl
449	3-$NH_2CH_2C_6H_4CH_2$	4-HOC_6H_4

450	3-$NH_2CH_2C_6H_4CH_2$	3-HOC_6H_4
451	3-$NH_2CH_2C_6H_4CH_2$	3,4-diHOC_6H_4
452	3-$NH_2CH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
453	3-$NH_2CH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
454	4-$NH_2CH_2C_6H_4CH_2$	4-$MeOC_6H_4$
455	4-$NH_2CH_2C_6H_4CH_2$	3-$MeOC_6H_4$
456	4-$NH_2CH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
457	4-$NH_2CH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
458	4-$NH_2CH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
459	4-$NH_2CH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
460	4-$NH_2CH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
461	4-$NH_2CH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
462	4-$NH_2CH_2C_6H_4CH_2$	4-pyridyl
463	4-$NH_2CH_2C_6H_4CH_2$	3-pyridyl
464	4-$NH_2CH_2C_6H_4CH_2$	2-pyridyl
465	4-$NH_2CH_2C_6H_4CH_2$	2-thiazolyl
466	4-$NH_2CH_2C_6H_4CH_2$	2-pyrazolyl
467	4-$NH_2CH_2C_6H_4CH_2$	5-isoquinolyl
468	4-$NH_2CH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
469	4-$NH_2CH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
470	4-$NH_2CH_2C_6H_4CH_2$	2-imidazolyl
471	4-$NH_2CH_2C_6H_4CH_2$	2-oxazolyl
472	4-$NH_2CH_2C_6H_4CH_2$	4-isoxazolyl
473	4-$NH_2CH_2C_6H_4CH_2$	4-HOC_6H_4
474	4-$NH_2CH_2C_6H_4CH_2$	3-HOC_6H_4
475	4-$NH_2CH_2C_6H_4CH_2$	3,4-diHOC_6H_4
476	4-$NH_2CH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$

477	4-$NH_2CH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
478	2-$Me_2NCH_2C_6H_4CH_2$	4-$MeOC_6H_4$
479	2-$Me_2NCH_2C_6H_4CH_2$	3-$MeOC_6H_4$
480	2-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
481	2-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
482	2-$Me_2NCH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
483	2-$Me_2NCH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
484	2-$Me_2NCH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
485	2-$Me_2NCH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
486	2-$Me_2NCH_2C_6H_4CH_2$	4-pyridyl
487	2-$Me_2NCH_2C_6H_4CH_2$	3-pyridyl
488	2-$Me_2NCH_2C_6H_4CH_2$	2-pyridyl
489	2-$Me_2NCH_2C_6H_4CH_2$	2-thiazolyl
490	2-$Me_2NCH_2C_6H_4CH_2$	2-pyrazolyl
491	2-$Me_2NCH_2C_6H_4CH_2$	5-isoquinolyl
492	2-$Me_2NCH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
493	2-$Me_2NCH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
494	2-$Me_2NCH_2C_6H_4CH_2$	2-imidazolyl
495	2-$Me_2NCH_2C_6H_4CH_2$	2-oxazolyl
496	2-$Me_2NCH_2C_6H_4CH_2$	4-isoxazolyl
497	2-$Me_2NCH_2C_6H_4CH_2$	4-HOC_6H_4
498	2-$Me_2NCH_2C_6H_4CH_2$	3-HOC_6H_4
499	2-$Me_2NCH_2C_6H_4CH_2$	3,4-diHOC_6H_4
500	2-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
501	2-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
502	3-$Me_2NCH_2C_6H_4CH_2$	4-$MeOC_6H_4$
503	3-$Me_2NCH_2C_6H_4CH_2$	3-$MeOC_6H_4$

504	3-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
505	3-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
506	3-$Me_2NCH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
507	3-$Me_2NCH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
508	3-$Me_2NCH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
509	3-$Me_2NCH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
510	3-$Me_2NCH_2C_6H_4CH_2$	4-pyridyl
511	3-$Me_2NCH_2C_6H_4CH_2$	3-pyridyl
512	3-$Me_2NCH_2C_6H_4CH_2$	2-pyridyl
513	3-$Me_2NCH_2C_6H_4CH_2$	2-thiazolyl
514	3-$Me_2NCH_2C_6H_4CH_2$	2-pyrazolyl
515	3-$Me_2NCH_2C_6H_4CH_2$	5-isoquinolyl
516	3-$Me_2NCH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
517	3-$Me_2NCH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
518	3-$Me_2NCH_2C_6H_4CH_2$	2-imidazolyl
519	3-$Me_2NCH_2C_6H_4CH_2$	2-oxazolyl
520	3-$Me_2NCH_2C_6H_4CH_2$	4-isoxazolyl
521	3-$Me_2NCH_2C_6H_4CH_2$	4-HOC_6H_4
522	3-$Me_2NCH_2C_6H_4CH_2$	3-HOC_6H_4
523	3-$Me_2NCH_2C_6H_4CH_2$	3,4-diHOC_6H_4
524	3-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
525	3-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
526	4-$Me_2NCH_2C_6H_4CH_2$	4-$MeOC_6H_4$
527	4-$Me_2NCH_2C_6H_4CH_2$	3-$MeOC_6H_4$
528	4-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
529	4-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
530	4-$Me_2NCH_2C_6H_4CH_2$	2-$NH_2C_6H_4$

	531	4-$Me_2NCH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	532	4-$Me_2NCH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	533	4-$Me_2NCH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	534	4-$Me_2NCH_2C_6H_4CH_2$	4-pyridyl
	535	4-$Me_2NCH_2C_6H_4CH_2$	3-pyridyl
	536	4-$Me_2NCH_2C_6H_4CH_2$	2-pyridyl
	537	4-$Me_2NCH_2C_6H_4CH_2$	2-thiazolyl
	538	4-$Me_2NCH_2C_6H_4CH_2$	2-pyrazolyl
	539	4-$Me_2NCH_2C_6H_4CH_2$	5-isoquinolyl
	540	4-$Me_2NCH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	541	4-$Me_2NCH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	542	4-$Me_2NCH_2C_6H_4CH_2$	2-imidazolyl
	543	4-$Me_2NCH_2C_6H_4CH_2$	2-oxazolyl
	545	4-$Me_2NCH_2C_6H_4CH_2$	4-isoxazolyl
	546	4-$Me_2NCH_2C_6H_4CH_2$	4-HOC_6H_4
	547	4-$Me_2NCH_2C_6H_4CH_2$	3-HOC_6H_4
	548	4-$Me_2NCH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	549	4-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	550	4-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	551	H	3-$MeOC_6H_4$
	552	H	4-$NH_2C_6H_4$
	553	H	3-$NH_2C_6H_4$
	554	H	2-$NH_2C_6H_4$
	555	H	4-$Me_2NC_6H_4$
	556	H	3-$Me_2NC_6H_4$
	557	H	2-$Me_2NC_6H_4$
	558	H	3-pyridyl

559	H	2-pyridyl
560	H	2-thiazolyl
561	H	2-pyrazolyl
562	H	5-isoquinolyl
563	H	3,4-methylenedioxyC_6H_3
564	H	3,4-ethylenedioxyC_6H_3
565	H	2-imidazolyl
566	H	2-oxazolyl
567	H	4-isoxazolyl
568	H	4-HOC_6H_4
569	H	3-HOC_6H_4
570	H	3,4-diHOC_6H_4
571	H	4-$NH_2CH_2C_6H_4$
572	H	3-$NH_2CH_2C_6H_4$
573	Me	3-$MeOC_6H_4$
574	Me	4-$NH_2C_6H_4$
575	Me	3-$NH_2C_6H_4$
576	Me	2-$NH_2C_6H_4$
577	Me	4-$Me_2NC_6H_4$
578	Me	3-$Me_2NC_6H_4$
579	Me	2-$Me_2NC_6H_4$
580	Me	3-pyridyl
581	Me	2-pyridyl
582	Me	2-thiazolyl
583	Me	2-pyrazolyl
584	Me	5-isoquinolyl
585	Me	3,4-ethylenedioxyC_6H_3
586	Me	2-imidazolyl

587	Me	2-oxazolyl
588	Me	4-isoxazolyl
589	Me	3-HOC_6H_4
590	Me	3,4-diHOC_6H_4
591	Me	4-$NH_2CH_2C_6H_4$
592	Me	3-$NH_2CH_2C_6H_4$
593	Et	3-$MeOC_6H_4$
594	Et	4-$NH_2C_6H_4$
595	Et	3-$NH_2C_6H_4$
596	Et	2-$NH_2C_6H_4$
597	Et	4-$Me_2NC_6H_4$
598	Et	3-$Me_2NC_6H_4$
599	Et	2-$Me_2NC_6H_4$
600	Et	4-pyridyl
601	Et	3-pyridyl
601	Et	2-pyridyl
603	Et	2-thiazolyl
604	Et	2-pyrazolyl
605	Et	5-isoquinolyl
606	Et	3,4-methylenedioxyC_6H_3
607	Et	3,4-ethylenedioxyC_6H_3
608	Et	2-imidazolyl
609	Et	2-oxazolyl
610	Et	4-isoxazolyl
611	Et	4-HOC_6H_4
612	Et	3-HOC_6H_4
613	Et	3,4-diHOC_6H_4
614	Et	4-$NH_2CH_2C_6H_4$

615	Et	3-$NH_2CH_2C_6H_4$
616	Me_2NCH_2	3-$MeOC_6H_4$
617	Me_2NCH_2	4-$NH_2C_6H_4$
618	Me_2NCH_2	3-$NH_2C_6H_4$
619	Me_2NCH_2	2-$NH_2C_6H_4$
620	Me_2NCH_2	4-$Me_2NC_6H_4$
621	Me_2NCH_2	3-$Me_2NC_6H_4$
622	Me_2NCH_2	2-$Me_2NC_6H_4$
623	Me_2NCH_2	4-pyridyl
624	Me_2NCH_2	3-pyridyl
625	Me_2NCH_2	2-pyridyl
626	Me_2NCH_2	2-thiazolyl
627	Me_2NCH_2	2-pyrazolyl
628	Me_2NCH_2	5-isoquinolyl
629	Me_2NCH_2	3,4-methylenedioxyC_6H_3
630	Me_2NCH_2	3,4-ethylenedioxyC_6H_3
631	Me_2NCH_2	2-imidazolyl
632	Me_2NCH_2	2-oxazolyl
633	Me_2NCH_2	4-isoxazolyl
634	Me_2NCH_2	4-HOC_6H_4
635	Me_2NCH_2	3-HOC_6H_4
636	Me_2NCH_2	3,4-diHOC_6H_4
637	Me_2NCH_2	4-$NH_2CH_2C_6H_4$
638	Me_2NCH_2	3-$NH_2CH_2C_6H_4$
639	$EtNHCH_2$	3-$MeOC_6H_4$
640	$EtNHCH_2$	4-$NH_2C_6H_4$
641	$EtNHCH_2$	3-$NH_2C_6H_4$

642	$EtNHCH_2$	$2\text{-}NH_2C_6H_4$
643	$EtNHCH_2$	$4\text{-}Me_2NC_6H_4$
644	$EtNHCH_2$	$3\text{-}Me_2NC_6H_4$
645	$EtNHCH_2$	$2\text{-}Me_2NC_6H_4$
646	$EtNHCH_2$	4-pyridyl
647	$EtNHCH_2$	3-pyridyl
648	$EtNHCH_2$	2-pyridyl
649	$EtNHCH_2$	2-thiazolyl
650	$EtNHCH_2$	2-pyrazolyl
651	$EtNHCH_2$	5-isoquinolyl
652	$EtNHCH_2$	3,4-methylenedioxyC_6H_3
653	$EtNHCH_2$	3,4-ethylenedioxyC_6H_3
654	$EtNHCH_2$	2-imidazolyl
655	$EtNHCH_2$	2-oxazolyl
656	$EtNHCH_2$	4-isoxazolyl
657	$EtNHCH_2$	$4\text{-}HOC_6H_4$
658	$EtNHCH_2$	$3\text{-}HOC_6H_4$
659	$EtNHCH_2$	$3,4\text{-}diHOC_6H_4$
660	$EtNHCH_2$	$4\text{-}NH_2CH_2C_6H_4$
661	$EtNHCH_2$	$3\text{-}NH_2CH_2C_6H_4$
662	$HOCH_2CH_2NHCH_2$	$3\text{-}MeOC_6H_4$
663	$HOCH_2CH_2NHCH_2$	$4\text{-}NH_2C_6H_4$
664	$HOCH_2CH_2NHCH_2$	$3\text{-}NH_2C_6H_4$
665	$HOCH_2CH_2NHCH_2$	$2\text{-}NH_2C_6H_4$
666	$HOCH_2CH_2NHCH_2$	$4\text{-}Me_2NC_6H_4$
667	$HOCH_2CH_2NHCH_2$	$3\text{-}Me_2NC_6H_4$
668	$HOCH_2CH_2NHCH_2$	$2\text{-}Me_2NC_6H_4$

669	$HOCH_2CH_2NHCH_2$	4-pyridyl
670	$HOCH_2CH_2NHCH_2$	3-pyridyl
671	$HOCH_2CH_2NHCH_2$	2-pyridyl
672	$HOCH_2CH_2NHCH_2$	2-thiazolyl
673	$HOCH_2CH_2NHCH_2$	2-pyrazolyl
674	$HOCH_2CH_2NHCH_2$	5-isoquinolyl
675	$HOCH_2CH_2NHCH_2$	3,4-methylenedioxyC_6H_3
676	$HOCH_2CH_2NHCH_2$	3,4-ethylenedioxyC_6H_3
677	$HOCH_2CH_2NHCH_2$	2-imidazolyl
678	$HOCH_2CH_2NHCH_2$	2-oxazolyl
679	$HOCH_2CH_2NHCH_2$	4-isoxazolyl
680	$HOCH_2CH_2NHCH_2$	4-HOC_6H_4
681	$HOCH_2CH_2NHCH_2$	3-HOC_6H_4
682	$HOCH_2CH_2NHCH_2$	3,4-diHOC_6H_4
683	$HOCH_2CH_2NHCH_2$	4-$NH_2CH_2C_6H_4$
684	$HOCH_2CH_2NHCH_2$	3-$NH_2CH_2C_6H_4$
685	$H_2NCH_2CH_2NHCH_2$	4-$MeOC_6H_4$
686	$H_2NCH_2CH_2NHCH_2$	3-$MeOC_6H_4$
687	$H_2NCH_2CH_2NHCH_2$	4-$NH_2C_6H_4$
688	$H_2NCH_2CH_2NHCH_2$	3-$NH_2C_6H_4$
689	$H_2NCH_2CH_2NHCH_2$	2-$NH_2C_6H_4$
690	$H_2NCH_2CH_2NHCH_2$	4-$Me_2NC_6H_4$
691	$H_2NCH_2CH_2NHCH_2$	3-$Me_2NC_6H_4$
692	$H_2NCH_2CH_2NHCH_2$	2-$Me_2NC_6H_4$
693	$H_2NCH_2CH_2NHCH_2$	4-pyridyl
694	$H_2NCH_2CH_2NHCH_2$	3-pyridyl
695	$H_2NCH_2CH_2NHCH_2$	2-pyridyl

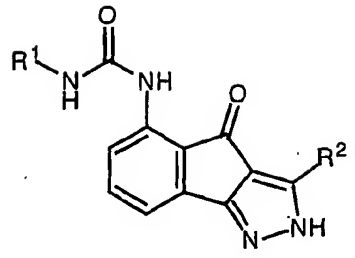
696	$H_2NCH_2CH_2NHCH_2$	2-thiazolyl
697	$H_2NCH_2CH_2NHCH_2$	2-pyrazolyl
698	$H_2NCH_2CH_2NHCH_2$	5-isoquinolyl
699	$H_2NCH_2CH_2NHCH_2$	3,4-methylenedioxyC_6H_3
700	$H_2NCH_2CH_2NHCH_2$	3,4-ethylenedioxyC_6H_3
701	$H_2NCH_2CH_2NHCH_2$	2-imidazolyl
702	$H_2NCH_2CH_2NHCH_2$	2-oxazolyl
703	$H_2NCH_2CH_2NHCH_2$	4-isoxazolyl
704	$H_2NCH_2CH_2NHCH_2$	4-HOC_6H_4
705	$H_2NCH_2CH_2NHCH_2$	3-HOC_6H_4
706	$H_2NCH_2CH_2NHCH_2$	3,4-diHOC_6H_4
707	$H_2NCH_2CH_2NHCH_2$	4-$NH_2CH_2C_6H_4$
708	$H_2NCH_2CH_2NHCH_2$	3-$NH_2CH_2C_6H_4$
709	$Me_2NCH_2CH_2NHCH_2$	4-$MeOC_6H_4$
710	$Me_2NCH_2CH_2NHCH_2$	3-$MeOC_6H_4$
711	$Me_2NCH_2CH_2NHCH_2$	4-$NH_2C_6H_4$
712	$Me_2NCH_2CH_2NHCH_2$	3-$NH_2C_6H_4$
713	$Me_2NCH_2CH_2NHCH_2$	2-$NH_2C_6H_4$
714	$Me_2NCH_2CH_2NHCH_2$	4-$Me_2NC_6H_4$
715	$Me_2NCH_2CH_2NHCH_2$	3-$Me_2NC_6H_4$
716	$Me_2NCH_2CH_2NHCH_2$	2-$Me_2NC_6H_4$
717	$Me_2NCH_2CH_2NHCH_2$	4-pyridyl
718	$Me_2NCH_2CH_2NHCH_2$	3-pyridyl
719	$Me_2NCH_2CH_2NHCH_2$	2-pyridyl
720	$Me_2NCH_2CH_2NHCH_2$	2-thiazolyl
721	$Me_2NCH_2CH_2NHCH_2$	2-pyrazolyl
722	$Me_2NCH_2CH_2NHCH_2$	5-isoquinolyl

	723	$Me_2NCH_2CH_2NHCH_2$	3,4-methylenedioxyC_6H_3
	724	$Me_2NCH_2CH_2NHCH_2$	3,4-ethylenedioxyC_6H_3
	725	$Me_2NCH_2CH_2NHCH_2$	2-imidazolyl
	726	$Me_2NCH_2CH_2NHCH_2$	2-oxazolyl
	727	$Me_2NCH_2CH_2NHCH_2$	4-isoxazolyl
	728	$Me_2NCH_2CH_2NHCH_2$	4-HOC_6H_4
	729	$Me_2NCH_2CH_2NHCH_2$	3-HOC_6H_4
	730	$Me_2NCH_2CH_2NHCH_2$	3,4-diHOC_6H_4
	731	$Me_2NCH_2CH_2NHCH_2$	4-$NH_2CH_2C_6H_4$
	732	$Me_2NCH_2CH_2NHCH_2$	3-$NH_2CH_2C_6H_4$
	733	1-morpholinylmethyl	3-$MeOC_6H_4$
	734	1-morpholinylmethyl	4-$NH_2C_6H_4$
	735	1-morpholinylmethyl	3-$NH_2C_6H_4$
	736	1-morpholinylmethyl	2-$NH_2C_6H_4$
	737	1-morpholinylmethyl	4-$Me_2NC_6H_4$
	738	1-morpholinylmethyl	3-$Me_2NC_6H_4$
	739	1-morpholinylmethyl	2-$Me_2NC_6H_4$
	740	1-morpholinylmethyl	4-pyridyl
	741	1-morpholinylmethyl	3-pyridyl
	742	1-morpholinylmethyl	2-pyridyl
	743	1-morpholinylmethyl	2-thiazolyl
	744	1-morpholinylmethyl	2-pyrazolyl
	745	1-morpholinylmethyl	5-isoquinolyl
	746	1-morpholinylmethyl	3,4-methylenedioxyC_6H_3
	747	1-morpholinylmethyl	3,4-ethylenedioxyC_6H_3
	748	1-morpholinylmethyl	2-imidazolyl

749	1-morpholinylmethyl	2-oxazolyl
750	1-morpholinylmethyl	4-isoxazolyl
751	1-morpholinylmethyl	4-HOC_6H_4
752	1-morpholinylmethyl	3-HOC_6H_4
753	1-morpholinylmethyl	3,4-diHOC_6H_4
754	1-morpholinylmethyl	4-$NH_2CH_2C_6H_4$
755	1-morpholinylmethyl	3-$NH_2CH_2C_6H_4$
756	1-thiomorpholinylmethyl	3-$MeOC_6H_4$
757	1-thiomorpholinylmethyl	4-$NH_2C_6H_4$
758	1-thiomorpholinylmethyl	3-$NH_2C_6H_4$
759	1-thiomorpholinylmethyl	2-$NH_2C_6H_4$
760	1-thiomorpholinylmethyl	4-$Me_2NC_6H_4$
761	1-thiomorpholinylmethyl	3-$Me_2NC_6H_4$
762	1-thiomorpholinylmethyl	2-$Me_2NC_6H_4$
763	1-thiomorpholinylmethyl	4-pyridyl
764	1-thiomorpholinylmethyl	3-pyridyl
765	1-thiomorpholinylmethyl	2-pyridyl
766	1-thiomorpholinylmethyl	2-thiazolyl
767	1-thiomorpholinylmethyl	2-pyrazolyl
768	1-thiomorpholinylmethyl	5-isoquinolyl
769	1-thiomorpholinylmethyl	3,4-methylenedioxyC_6H_3
770	1-thiomorpholinylmethyl	3,4-ethylenedioxyC_6H_3
771	1-thiomorpholinylmethyl	2-imidazolyl
772	1-thiomorpholinylmethyl	2-oxazolyl
773	1-thiomorpholinylmethyl	4-isoxazolyl
774	1-thiomorpholinylmethyl	4-HOC_6H_4
775	1-thiomorpholinylmethyl	3-HOC_6H_4
776	1-thiomorpholinylmethyl	3,4-diHOC_6H_4

	777	1-thiomorpholinylmethyl	4-$NH_2CH_2C_6H_4$
	778	1-thiomorpholinylmethyl	3-$NH_2CH_2C_6H_4$
	779	1-piperazinylmethyl	3-$MeOC_6H_4$
	780	1-piperazinylmethyl	4-$NH_2C_6H_4$
	781	1-piperazinylmethyl	3-$NH_2C_6H_4$
	782	1-piperazinylmethyl	2-$NH_2C_6H_4$
	783	1-piperazinylmethyl	4-$Me_2NC_6H_4$
	784	1-piperazinylmethyl	3-$Me_2NC_6H_4$
	785	1-piperazinylmethyl	2-$Me_2NC_6H_4$
	786	1-piperazinylmethyl	4-pyridyl
	787	1-piperazinylmethyl	3-pyridyl
	788	1-piperazinylmethyl	2-pyridyl
	789	1-piperazinylmethyl	2-thiazolyl
	790	1-piperazinylmethyl	2-pyrazolyl
	791	1-piperazinylmethyl	5-isoquinolyl
	792	1-piperazinylmethyl	3,4-methylenedioxyC_6H_3
	793	1-piperazinylmethyl	3,4-ethylenedioxyC_6H_3
	794	1-piperazinylmethyl	2-imidazolyl
	795	1-piperazinylmethyl	2-oxazolyl
	796	1-piperazinylmethyl	4-isoxazolyl
	797	1-piperazinylmethyl	4-HOC_6H_4
	798	1-piperazinylmethyl	3-HOC_6H_4
	799	1-piperazinylmethyl	3,4-diHOC_6H_4
	800	1-piperazinylmethyl	4-$NH_2CH_2C_6H_4$
	801	1-piperazinylmethyl	3-$NH_2CH_2C_6H_4$

Table 3



Example Number	R^1	R^2
802	2-pyridylmethyl	4-$MeOC_6H_4$
803	2-pyridylmethyl	3-$MeOC_6H_4$
804	2-pyridylmethyl	4-$NH_2C_6H_4$
805	2-pyridylmethyl	3-$NH_2C_6H_4$
806	2-pyridylmethyl	2-$NH_2C_6H_4$
807	2-pyridylmethyl	4-$Me_2NC_6H_4$
808	2-pyridylmethyl	3-$Me_2NC_6H_4$
809	2-pyridylmethyl	2-$Me_2NC_6H_4$
810	2-pyridylmethyl	4-pyridyl
811	2-pyridylmethyl	3-pyridyl
812	2-pyridylmethyl	2-pyridyl
813	2-pyridylmethyl	2-thiazolyl
814	2-pyridylmethyl	2-pyrazolyl
815	2-pyridylmethyl	5-isoquinolyl
816	2-pyridylmethyl	3,4-methylenedioxyC_6H_3
817	2-pyridylmethyl	3,4-ethylenedioxyC_6H_3
818	2-pyridylmethyl	2-imidazolyl
819	2-pyridylmethyl	2-oxazolyl
820	2-pyridylmethyl	4-isoxazolyl
821	2-pyridylmethyl	4-HOC_6H_4

822	2-pyridylmethyl	3-HOC_6H_4
823	2-pyridylmethyl	3,4-diHOC_6H_4
824	2-pyridylmethyl	4-$NH_2CH_2C_6H_4$
825	2-pyridylmethyl	3-$NH_2CH_2C_6H_4$
826	3-pyridylmethyl	4-$MeOC_6H_4$
827	3-pyridylmethyl	3-$MeOC_6H_4$
828	3-pyridylmethyl	4-$NH_2C_6H_4$
829	3-pyridylmethyl	3-$NH_2C_6H_4$
830	3-pyridylmethyl	2-$NH_2C_6H_4$
831	3-pyridylmethyl	4-$Me_2NC_6H_4$
832	3-pyridylmethyl	3-$Me_2NC_6H_4$
833	3-pyridylmethyl	2-$Me_2NC_6H_4$
834	3-pyridylmethyl	4-pyridyl
835	3-pyridylmethyl	3-pyridyl
836	3-pyridylmethyl	2-pyridyl
837	3-pyridylmethyl	2-thiazolyl
838	3-pyridylmethyl	2-pyrazolyl
839	3-pyridylmethyl	5-isoquinolyl
840	3-pyridylmethyl	3,4-methylenedioxyC_6H_3
841	3-pyridylmethyl	3,4-ethylenedioxyC_6H_3
842	3-pyridylmethyl	2-imidazolyl
843	3-pyridylmethyl	2-oxazolyl
844	3-pyridylmethyl	4-isoxazolyl
845	3-pyridylmethyl	4-HOC_6H_4
846	3-pyridylmethyl	3-HOC_6H_4
847	3-pyridylmethyl	3,4-diHOC_6H_4
848	3-pyridylmethyl	4-$NH_2CH_2C_6H_4$
849	3-pyridylmethyl	3-$NH_2CH_2C_6H_4$

	850	4-pyridylmethyl	4-$MeOC_6H_4$
	851	4-pyridylmethyl	3-$MeOC_6H_4$
	852	4-pyridylmethyl	4-$NH_2C_6H_4$
	853	4-pyridylmethyl	3-$NH_2C_6H_4$
	854	4-pyridylmethyl	2-$NH_2C_6H_4$
	855	4-pyridylmethyl	4-$Me_2NC_6H_4$
	856	4-pyridylmethyl	3-$Me_2NC_6H_4$
	857	4-pyridylmethyl	2-$Me_2NC_6H_4$
	858	4-pyridylmethyl	4-pyridyl
	859	4-pyridylmethyl	3-pyridyl
	860	4-pyridylmethyl	2-pyridyl
	861	4-pyridylmethyl	2-thiazolyl
	862	4-pyridylmethyl	2-pyrazolyl
	863	4-pyridylmethyl	5-isoquinolyl
	864	4-pyridylmethyl	3,4-methylenedioxyC_6H_3
	865	4-pyridylmethyl	3,4-ethylenedioxyC_6H_3
	866	4-pyridylmethyl	2-imidazolyl
	867	4-pyridylmethyl	2-oxazolyl
	868	4-pyridylmethyl	4-isoxazolyl
	869	4-pyridylmethyl	4-HOC_6H_4
	870	4-pyridylmethyl	3-HOC_6H_4
	871	4-pyridylmethyl	3,4-diHOC_6H_4
	872	4-pyridylmethyl	4-$NH_2CH_2C_6H_4$
	873	4-pyridylmethyl	3-$NH_2CH_2C_6H_4$
	874	2-$NH_2C_6H_4$	4-$MeOC_6H_4$
	875	2-$NH_2C_6H_4$	3-$MeOC_6H_4$
	876	2-$NH_2C_6H_4$	4-$NH_2C_6H_4$
	877	2-$NH_2C_6H_4$	3-$NH_2C_6H_4$

	878	2-$NH_2C_6H_4$	2-$NH_2C_6H_4$
	879	2-$NH_2C_6H_4$	4-$Me_2NC_6H_4$
	880	2-$NH_2C_6H_4$	3-$Me_2NC_6H_4$
	881	2-$NH_2C_6H_4$	2-$Me_2NC_6H_4$
	882	2-$NH_2C_6H_4$	4-pyridyl
	883	2-$NH_2C_6H_4$	3-pyridyl
	884	2-$NH_2C_6H_4$	2-pyridyl
	885	2-$NH_2C_6H_4$	2-thiazolyl
	886	2-$NH_2C_6H_4$	2-pyrazolyl
	887	2-$NH_2C_6H_4$	5-isoquinolyl
	888	2-$NH_2C_6H_4$	3,4-methylenedioxyC_6H_3
	889	2-$NH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
	890	2-$NH_2C_6H_4$	2-imidazolyl
	891	2-$NH_2C_6H_4$	2-oxazolyl
	892	2-$NH_2C_6H_4$	4-isoxazolyl
	893	2-$NH_2C_6H_4$	4-HOC_6H_4
	894	2-$NH_2C_6H_4$	3-HOC_6H_4
	895	2-$NH_2C_6H_4$	3,4-diHOC_6H_4
	896	2-$NH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
	897	2-$NH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
	898	3-$NH_2C_6H_4$	4-$MeOC_6H_4$
	899	3-$NH_2C_6H_4$	3-$MeOC_6H_4$
	900	3-$NH_2C_6H_4$	4-$NH_2C_6H_4$
	901	3-$NH_2C_6H_4$	3-$NH_2C_6H_4$
	902	3-$NH_2C_6H_4$	2-$NH_2C_6H_4$
	903	3-$NH_2C_6H_4$	4-$Me_2NC_6H_4$
	904	3-$NH_2C_6H_4$	3-$Me_2NC_6H_4$

905	3-$NH_2C_6H_4$	2-$Me_2NC_6H_4$
906	3-$NH_2C_6H_4$	4-pyridyl
907	3-$NH_2C_6H_4$	3-pyridyl
908	3-$NH_2C_6H_4$	2-pyridyl
909	3-$NH_2C_6H_4$	2-thiazolyl
910	3-$NH_2C_6H_4$	2-pyrazolyl
911	3-$NH_2C_6H_4$	5-isoquinolyl
912	3-$NH_2C_6H_4$	3,4-methylenedioxyC_6H_3
913	3-$NH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
914	3-$NH_2C_6H_4$	2-imidazolyl
915	3-$NH_2C_6H_4$	2-oxazolyl
916	3-$NH_2C_6H_4$	4-isoxazolyl
917	3-$NH_2C_6H_4$	4-HOC_6H_4
918	3-$NH_2C_6H_4$	3-HOC_6H_4
919	3-$NH_2C_6H_4$	3,4-diHOC_6H_4
920	3-$NH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
921	3-$NH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
922	4-$NH_2C_6H_4$	4-$MeOC_6H_4$
923	4-$NH_2C_6H_4$	3-$MeOC_6H_4$
924	4-$NH_2C_6H_4$	4-$NH_2C_6H_4$
925	4-$NH_2C_6H_4$	3-$NH_2C_6H_4$
926	4-$NH_2C_6H_4$	2-$NH_2C_6H_4$
927	4-$NH_2C_6H_4$	4-$Me_2NC_6H_4$
928	4-$NH_2C_6H_4$	3-$Me_2NC_6H_4$
930	4-$NH_2C_6H_4$	2-$Me_2NC_6H_4$
931	4-$NH_2C_6H_4$	4-pyridyl
932	4-$NH_2C_6H_4$	3-pyridyl

	933	4-$NH_2C_6H_4$	2-pyridyl
	934	4-$NH_2C_6H_4$	2-thiazolyl
	935	4-$NH_2C_6H_4$	2-pyrazolyl
	936	4-$NH_2C_6H_4$	5-isoquinolyl
	937	4-$NH_2C_6H_4$	3,4-methylenedioxyC_6H_3
	938	4-$NH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
	939	4-$NH_2C_6H_4$	2-imidazolyl
	940	4-$NH_2C_6H_4$	2-oxazolyl
	941	4-$NH_2C_6H_4$	4-isoxazolyl
	942	4-$NH_2C_6H_4$	4-HOC_6H_4
	943	4-$NH_2C_6H_4$	3-HOC_6H_4
	944	4-$NH_2C_6H_4$	3,4-diHOC_6H_4
	945	4-$NH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
	946	4-$NH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
	947	2-$MeOC_6H_4$	4-$MeOC_6H_4$
	948	2-$MeOC_6H_4$	3-$MeOC_6H_4$
	949	2-$MeOC_6H_4$	4-$NH_2C_6H_4$
	950	2-$MeOC_6H_4$	3-$NH_2C_6H_4$
	951	2-$MeOC_6H_4$	2-$NH_2C_6H_4$
	952	2-$MeOC_6H_4$	4-$Me_2NC_6H_4$
	953	2-$MeOC_6H_4$	3-$Me_2NC_6H_4$
	954	2-$MeOC_6H_4$	2-$Me_2NC_6H_4$
	955	2-$MeOC_6H_4$	4-pyridyl
	956	2-$MeOC_6H_4$	3-pyridyl
	957	2-$MeOC_6H_4$	2-pyridyl
	958	2-$MeOC_6H_4$	2-thiazolyl
	959	2-$MeOC_6H_4$	2-pyrazolyl

960	2-$MeOC_6H_4$	5-isoquinolyl
961	2-$MeOC_6H_4$	3,4-methylenedioxyC_6H_3
962	2-$MeOC_6H_4$	3,4-ethylenedioxyC_6H_3
963	2-$MeOC_6H_4$	2-imidazolyl
964	2-$MeOC_6H_4$	2-oxazolyl
965	2-$MeOC_6H_4$	4-isoxazolyl
966	2-$MeOC_6H_4$	4-HOC_6H_4
967	2-$MeOC_6H_4$	3-HOC_6H_4
968	2-$MeOC_6H_4$	3,4-diHOC_6H_4
969	2-$MeOC_6H_4$	4-$NH_2CH_2C_6H_4$
970	2-$MeOC_6H_4$	3-$NH_2CH_2C_6H_4$
971	3-$MeOC_6H_4$	4-$MeOC_6H_4$
972	3-$MeOC_6H_4$	3-$MeOC_6H_4$
973	3-$MeOC_6H_4$	4-$NH_2C_6H_4$
974	3-$MeOC_6H_4$	3-$NH_2C_6H_4$
975	3-$MeOC_6H_4$	2-$NH_2C_6H_4$
976	3-$MeOC_6H_4$	4-$Me_2NC_6H_4$
977	3-$MeOC_6H_4$	3-$Me_2NC_6H_4$
978	3-$MeOC_6H_4$	2-$Me_2NC_6H_4$
979	3-$MeOC_6H_4$	4-pyridyl
980	3-$MeOC_6H_4$	3-pyridyl
981	3-$MeOC_6H_4$	2-pyridyl
982	3-$MeOC_6H_4$	2-thiazolyl
983	3-$MeOC_6H_4$	2-pyrazolyl
984	3-$MeOC_6H_4$	5-isoquinolyl
985	3-$MeOC_6H_4$	3,4-methylenedioxyC_6H_3

	986	3-$MeOC_6H_4$	3,4-ethylenedioxyC_6H_3
	987	3-$MeOC_6H_4$	2-imidazolyl
	988	3-$MeOC_6H_4$	2-oxazolyl
	989	3-$MeOC_6H_4$	4-isoxazolyl
	990	3-$MeOC_6H_4$	4-HOC_6H_4
	991	3-$MeOC_6H_4$	3-HOC_6H_4
	992	3-$MeOC_6H_4$	3,4-diHOC_6H_4
	993	3-$MeOC_6H_4$	4-$NH_2CH_2C_6H_4$
	994	3-$MeOC_6H_4$	3-$NH_2CH_2C_6H_4$
	995	4-$MeOC_6H_4$	4-$MeOC_6H_4$
	996	4-$MeOC_6H_4$	3-$MeOC_6H_4$
	997	4-$MeOC_6H_4$	4-$NH_2C_6H_4$
	998	4-$MeOC_6H_4$	3-$NH_2C_6H_4$
	999	4-$MeOC_6H_4$	2-$NH_2C_6H_4$
	1000	4-$MeOC_6H_4$	4-$Me_2NC_6H_4$
	1001	4-$MeOC_6H_4$	3-$Me_2NC_6H_4$
	1002	4-$MeOC_6H_4$	2-$Me_2NC_6H_4$
	1003	4-$MeOC_6H_4$	4-pyridyl
	1004	4-$MeOC_6H_4$	3-pyridyl
	1005	4-$MeOC_6H_4$	2-pyridyl
	1006	4-$MeOC_6H_4$	2-thiazolyl
	1007	4-$MeOC_6H_4$	2-pyrazolyl
	1008	4-$MeOC_6H_4$	5-isoquinolyl
	1009	4-$MeOC_6H_4$	3,4-methylenedioxyC_6H_3
	1010	4-$MeOC_6H_4$	3,4-ethylenedioxyC_6H_3
	1011	4-$MeOC_6H_4$	2-imidazolyl

1012	4-$MeOC_6H_4$	2-oxazolyl
1013	4-$MeOC_6H_4$	4-isoxazolyl
1014	4-$MeOC_6H_4$	4-HOC_6H_4
1015	4-$MeOC_6H_4$	3-HOC_6H_4
1016	4-$MeOC_6H_4$	3,4-diHOC_6H_4
1017	4-$MeOC_6H_4$	4-$NH_2CH_2C_6H_4$
1018	4-$MeOC_6H_4$	3-$NH_2CH_2C_6H_4$
1019	2-HOC_6H_4	4-$MeOC_6H_4$
1020	2-HOC_6H_4	3-$MeOC_6H_4$
1021	2-HOC_6H_4	4-$NH_2C_6H_4$
1022	2-HOC_6H_4	3-$NH_2C_6H_4$
1023	2-HOC_6H_4	2-$NH_2C_6H_4$
1024	2-HOC_6H_4	4-$Me_2NC_6H_4$
1025	2-HOC_6H_4	3-$Me_2NC_6H_4$
1026	2-HOC_6H_4	2-$Me_2NC_6H_4$
1027	2-HOC_6H_4	4-pyridyl
1028	2-HOC_6H_4	3-pyridyl
1029	2-HOC_6H_4	2-pyridyl
1030	2-HOC_6H_4	2-thiazolyl
1031	2-HOC_6H_4	2-pyrazolyl
1032	2-HOC_6H_4	5-isoquinolyl
1033	2-HOC_6H_4	3,4-methylenedioxyC_6H_3
1034	2-HOC_6H_4	3,4-ethylenedioxyC_6H_3
1035	2-HOC_6H_4	2-imidazolyl
1036	2-HOC_6H_4	2-oxazolyl
1037	2-HOC_6H_4	4-isoxazolyl
1038	2-HOC_6H_4	4-HOC_6H_4

1039	2-HOC_6H_4	3-HOC_6H_4
1040	2-HOC_6H_4	3,4-diHOC_6H_4
1041	2-HOC_6H_4	4-$NH_2CH_2C_6H_4$
1042	2-HOC_6H_4	3-$NH_2CH_2C_6H_4$
1043	3-HOC_6H_4	4-$MeOC_6H_4$
1044	3-HOC_6H_4	3-$MeOC_6H_4$
1045	3-HOC_6H_4	4-$NH_2C_6H_4$
1046	3-HOC_6H_4	3-$NH_2C_6H_4$
1047	3-HOC_6H_4	2-$NH_2C_6H_4$
1048	3-HOC_6H_4	4-$Me_2NC_6H_4$
1049	3-HOC_6H_4	3-$Me_2NC_6H_4$
1050	3-HOC_6H_4	2-$Me_2NC_6H_4$
1051	3-HOC_6H_4	4-pyridyl
1052	3-HOC_6H_4	3-pyridyl
1053	3-HOC_6H_4	2-pyridyl
1054	3-HOC_6H_4	2-thiazolyl
1055	3-HOC_6H_4	2-pyrazolyl
1056	3-HOC_6H_4	5-isoquinolyl
1057	3-HOC_6H_4	3,4-methylenedioxyC_6H_3
1058	3-HOC_6H_4	3,4-ethylenedioxyC_6H_3
1059	3-HOC_6H_4	2-imidazolyl
1060	3-HOC_6H_4	2-oxazolyl
1061	3-HOC_6H_4	4-isoxazolyl
1062	3-HOC_6H_4	4-HOC_6H_4
1063	3-HOC_6H_4	3-HOC_6H_4
1064	3-HOC_6H_4	3,4-diHOC_6H_4
1065	3-HOC_6H_4	4-$NH_2CH_2C_6H_4$

1066	3-HOC_6H_4	3-$NH_2CH_2C_6H_4$
1067	4-HOC_6H_4	4-$MeOC_6H_4$
1068	4-HOC_6H_4	3-$MeOC_6H_4$
1069	4-HOC_6H_4	4-$NH_2C_6H_4$
1070	4-HOC_6H_4	3-$NH_2C_6H_4$
1071	4-HOC_6H_4	2-$NH_2C_6H_4$
1072	4-HOC_6H_4	4-$Me_2NC_6H_4$
1073	4-HOC_6H_4	3-$Me_2NC_6H_4$
1074	4-HOC_6H_4	2-$Me_2NC_6H_4$
1075	4-HOC_6H_4	4-pyridyl
1076	4-HOC_6H_4	3-pyridyl
1077	4-HOC_6H_4	2-pyridyl
1078	4-HOC_6H_4	2-thiazolyl
1079	4-HOC_6H_4	2-pyrazolyl
1080	4-HOC_6H_4	5-isoquinolyl
1081	4-HOC_6H_4	3,4-methylenedioxyC_6H_3
1082	4-HOC_6H_4	3,4-ethylenedioxyC_6H_3
1083	4-HOC_6H_4	2-imidazolyl
1084	4-HOC_6H_4	2-oxazolyl
1085	4-HOC_6H_4	4-isoxazolyl
1086	4-HOC_6H_4	4-HOC_6H_4
1087	4-HOC_6H_4	3-HOC_6H_4
1088	4-HOC_6H_4	3,4-diHOC_6H_4
1089	4-HOC_6H_4	4-$NH_2CH_2C_6H_4$
1090	4-HOC_6H_4	3-$NH_2CH_2C_6H_4$
1091	4-ClC_6H_4	4-$MeOC_6H_4$
1092	4-ClC_6H_4	3-$MeOC_6H_4$

1093	4-ClC_6H_4	4-$NH_2C_6H_4$
1094	4-ClC_6H_4	3-$NH_2C_6H_4$
1095	4-ClC_6H_4	2-$NH_2C_6H_4$
1096	4-ClC_6H_4	4-$Me_2NC_6H_4$
1097	4-ClC_6H_4	3-$Me_2NC_6H_4$
1098	4-ClC_6H_4	2-$Me_2NC_6H_4$
1099	4-ClC_6H_4	4-pyridyl
1100	4-ClC_6H_4	3-pyridyl
1101	4-ClC_6H_4	2-pyridyl
1102	4-ClC_6H_4	2-thiazolyl
1103	4-ClC_6H_4	2-pyrazolyl
1104	4-ClC_6H_4	5-isoquinolyl
1105	4-ClC_6H_4	3,4-methylenedioxyC_6H_3
1106	4-ClC_6H_4	3,4-ethylenedioxyC_6H_3
1107	4-ClC_6H_4	2-imidazolyl
1108	4-ClC_6H_4	2-oxazolyl
1109	4-ClC_6H_4	4-isoxazolyl
1110	4-ClC_6H_4	4-HOC_6H_4
1111	4-ClC_6H_4	3-HOC_6H_4
1112	4-ClC_6H_4	3,4-diHOC_6H_4
1113	4-ClC_6H_4	4-$NH_2CH_2C_6H_4$
1114	4-ClC_6H_4	3-$NH_2CH_2C_6H_4$
1115	2-$NH_2CH_2C_6H_4$	4-$MeOC_6H_4$
1116	2-$NH_2CH_2C_6H_4$	3-$MeOC_6H_4$
1117	2-$NH_2CH_2C_6H_4$	4-$NH_2C_6H_4$
1118	2-$NH_2CH_2C_6H_4$	3-$NH_2C_6H_4$
1119	2-$NH_2CH_2C_6H_4$	2-$NH_2C_6H_4$

1120	2-$NH_2CH_2C_6H_4$	4-$Me_2NC_6H_4$
1121	2-$NH_2CH_2C_6H_4$	3-$Me_2NC_6H_4$
1122	2-$NH_2CH_2C_6H_4$	2-$Me_2NC_6H_4$
1123	2-$NH_2CH_2C_6H_4$	4-pyridyl
1124	2-$NH_2CH_2C_6H_4$	3-pyridyl
1125	2-$NH_2CH_2C_6H_4$	2-pyridyl
1126	2-$NH_2CH_2C_6H_4$	2-thiazolyl
1127	2-$NH_2CH_2C_6H_4$	2-pyrazolyl
1128	2-$NH_2CH_2C_6H_4$	5-isoquinolyl
1129	2-$NH_2CH_2C_6H_4$	3,4-methylenedioxyC_6H_3
1130	2-$NH_2CH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
1131	2-$NH_2CH_2C_6H_4$	2-imidazolyl
1132	2-$NH_2CH_2C_6H_4$	2-oxazolyl
1133	2-$NH_2CH_2C_6H_4$	4-isoxazolyl
1134	2-$NH_2CH_2C_6H_4$	4-HOC_6H_4
1135	2-$NH_2CH_2C_6H_4$	3-HOC_6H_4
1136	2-$NH_2CH_2C_6H_4$	3,4-diHOC_6H_4
1137	2-$NH_2CH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
1138	2-$NH_2CH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
1139	3-$NH_2CH_2C_6H_4$	4-$MeOC_6H_4$
1140	3-$NH_2CH_2C_6H_4$	3-$MeOC_6H_4$
1141	3-$NH_2CH_2C_6H_4$	4-$NH_2C_6H_4$
1142	3-$NH_2CH_2C_6H_4$	3-$NH_2C_6H_4$
1143	3-$NH_2CH_2C_6H_4$	2-$NH_2C_6H_4$
1144	3-$NH_2CH_2C_6H_4$	4-$Me_2NC_6H_4$
1145	3-$NH_2CH_2C_6H_4$	3-$Me_2NC_6H_4$
1146	3-$NH_2CH_2C_6H_4$	2-$Me_2NC_6H_4$

	1147	3-$NH_2CH_2C_6H_4$	4-pyridyl
	1148	3-$NH_2CH_2C_6H_4$	3-pyridyl
	1149	3-$NH_2CH_2C_6H_4$	2-pyridyl
	1150	3-$NH_2CH_2C_6H_4$	2-thiazolyl
	1151	3-$NH_2CH_2C_6H_4$	2-pyrazolyl
	1152	3-$NH_2CH_2C_6H_4$	5-isoquinolyl
	1153	3-$NH_2CH_2C_6H_4$	3,4-methylenedioxyC_6H_3
	1154	3-$NH_2CH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
	1155	3-$NH_2CH_2C_6H_4$	2-imidazolyl
	1156	3-$NH_2CH_2C_6H_4$	2-oxazolyl
	1157	3-$NH_2CH_2C_6H_4$	4-isoxazolyl
	1158	3-$NH_2CH_2C_6H_4$	4-HOC_6H_4
	1159	3-$NH_2CH_2C_6H_4$	3-HOC_6H_4
	1160	3-$NH_2CH_2C_6H_4$	3,4-diHOC_6H_4
	1161	3-$NH_2CH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
	1162	3-$NH_2CH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
	1163	4-$NH_2CH_2C_6H_4$	4-$MeOC_6H_4$
	1164	4-$NH_2CH_2C_6H_4$	3-$MeOC_6H_4$
	1165	4-$NH_2CH_2C_6H_4$	4-$NH_2C_6H_4$
	1166	4-$NH_2CH_2C_6H_4$	3-$NH_2C_6H_4$
	1167	4-$NH_2CH_2C_6H_4$	2-$NH_2C_6H_4$
	1168	4-$NH_2CH_2C_6H_4$	4-$Me_2NC_6H_4$
	1169	4-$NH_2CH_2C_6H_4$	3-$Me_2NC_6H_4$
	1170	4-$NH_2CH_2C_6H_4$	2-$Me_2NC_6H_4$
	1171	4-$NH_2CH_2C_6H_4$	4-pyridyl
	1172	4-$NH_2CH_2C_6H_4$	3-pyridyl
	1173	4-$NH_2CH_2C_6H_4$	2-pyridyl

1174	4-$NH_2CH_2C_6H_4$	2-thiazolyl
1175	4-$NH_2CH_2C_6H_4$	2-pyrazolyl
1176	4-$NH_2CH_2C_6H_4$	5-isoquinolyl
1177	4-$NH_2CH_2C_6H_4$	3,4-methylenedioxyC_6H_3
1178	4-$NH_2CH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
1179	4-$NH_2CH_2C_6H_4$	2-imidazolyl
1180	4-$NH_2CH_2C_6H_4$	2-oxazolyl
1181	4-$NH_2CH_2C_6H_4$	4-isoxazolyl
1182	4-$NH_2CH_2C_6H_4$	4-HOC_6H_4
1183	4-$NH_2CH_2C_6H_4$	3-HOC_6H_4
1184	4-$NH_2CH_2C_6H_4$	3,4-diHOC_6H_4
1185	4-$NH_2CH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
1186	4-$NH_2CH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
1187	2-$Me_2NCH_2C_6H_4$	4-$MeOC_6H_4$
1188	2-$Me_2NCH_2C_6H_4$	3-$MeOC_6H_4$
1189	2-$Me_2NCH_2C_6H_4$	4-$NH_2C_6H_4$
1190	2-$Me_2NCH_2C_6H_4$	3-$NH_2C_6H_4$
1191	2-$Me_2NCH_2C_6H_4$	2-$NH_2C_6H_4$
1192	2-$Me_2NCH_2C_6H_4$	4-$Me_2NC_6H_4$
1193	2-$Me_2NCH_2C_6H_4$	3-$Me_2NC_6H_4$
1194	2-$Me_2NCH_2C_6H_4$	2-$Me_2NC_6H_4$
1195	2-$Me_2NCH_2C_6H_4$	4-pyridyl
1196	2-$Me_2NCH_2C_6H_4$	3-pyridyl
1197	2-$Me_2NCH_2C_6H_4$	2-pyridyl
1198	2-$Me_2NCH_2C_6H_4$	2-thiazolyl
1199	2-$Me_2NCH_2C_6H_4$	2-pyrazolyl
1200	2-$Me_2NCH_2C_6H_4$	5-isoquinolyl

	1201	2-$Me_2NCH_2C_6H_4$	3,4-methylenedioxyC_6H_3
	1202	2-$Me_2NCH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
	1203	2-$Me_2NCH_2C_6H_4$	2-imidazolyl
	1204	2-$Me_2NCH_2C_6H_4$	2-oxazolyl
	1205	2-$Me_2NCH_2C_6H_4$	4-isoxazolyl
	1206	2-$Me_2NCH_2C_6H_4$	4-HOC_6H_4
	1207	2-$Me_2NCH_2C_6H_4$	3-HOC_6H_4
	1208	2-$Me_2NCH_2C_6H_4$	3,4-diHOC_6H_4
	1209	2-$Me_2NCH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
	1210	2-$Me_2NCH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
	1211	3-$Me_2NCH_2C_6H_4$	4-$MeOC_6H_4$
	1212	3-$Me_2NCH_2C_6H_4$	3-$MeOC_6H_4$
	1213	3-$Me_2NCH_2C_6H_4$	4-$NH_2C_6H_4$
	1214	3-$Me_2NCH_2C_6H_4$	3-$NH_2C_6H_4$
	1215	3-$Me_2NCH_2C_6H_4$	2-$NH_2C_6H_4$
	1216	3-$Me_2NCH_2C_6H_4$	4-$Me_2NC_6H_4$
	1217	3-$Me_2NCH_2C_6H_4$	3-$Me_2NC_6H_4$
	1218	3-$Me_2NCH_2C_6H_4$	2-$Me_2NC_6H_4$
	1219	3-$Me_2NCH_2C_6H_4$	4-pyridyl
	1220	3-$Me_2NCH_2C_6H_4$	3-pyridyl
	1221	3-$Me_2NCH_2C_6H_4$	2-pyridyl
	1222	3-$Me_2NCH_2C_6H_4$	2-thiazolyl
	1223	3-$Me_2NCH_2C_6H_4$	2-pyrazolyl
	1224	3-$Me_2NCH_2C_6H_4$	5-isoquinolyl
	1225	3-$Me_2NCH_2C_6H_4$	3,4-methylenedioxyC_6H_3

1226	3-$Me_2NCH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
1227	3-$Me_2NCH_2C_6H_4$	2-imidazolyl
1228	3-$Me_2NCH_2C_6H_4$	2-oxazolyl
1229	3-$Me_2NCH_2C_6H_4$	4-isoxazolyl
1230	3-$Me_2NCH_2C_6H_4$	4-HOC_6H_4
1231	3-$Me_2NCH_2C_6H_4$	3-HOC_6H_4
1232	3-$Me_2NCH_2C_6H_4$	3,4-diHOC_6H_4
1233	3-$Me_2NCH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
1234	3-$Me_2NCH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
1235	4-$Me_2NCH_2C_6H_4$	4-$MeOC_6H_4$
1236	4-$Me_2NCH_2C_6H_4$	3-$MeOC_6H_4$
1237	4-$Me_2NCH_2C_6H_4$	4-$NH_2C_6H_4$
1238	4-$Me_2NCH_2C_6H_4$	3-$NH_2C_6H_4$
1239	4-$Me_2NCH_2C_6H_4$	2-$NH_2C_6H_4$
1240	4-$Me_2NCH_2C_6H_4$	4-$Me_2NC_6H_4$
1241	4-$Me_2NCH_2C_6H_4$	3-$Me_2NC_6H_4$
1242	4-$Me_2NCH_2C_6H_4$	2-$Me_2NC_6H_4$
1243	4-$Me_2NCH_2C_6H_4$	4-pyridyl
1244	4-$Me_2NCH_2C_6H_4$	3-pyridyl
1245	4-$Me_2NCH_2C_6H_4$	2-pyridyl
1246	4-$Me_2NCH_2C_6H_4$	2-thiazolyl
1247	4-$Me_2NCH_2C_6H_4$	2-pyrazolyl
1248	4-$Me_2NCH_2C_6H_4$	5-isoquinolyl
1249	4-$Me_2NCH_2C_6H_4$	3,4-methylenedioxyC_6H_3
1250	4-$Me_2NCH_2C_6H_4$	3,4-ethylenedioxyC_6H_3
1251	4-$Me_2NCH_2C_6H_4$	2-imidazolyl

	1252	4-$Me_2NCH_2C_6H_4$	2-oxazolyl
	1253	4-$Me_2NCH_2C_6H_4$	4-isoxazolyl
	1254	4-$Me_2NCH_2C_6H_4$	4-HOC_6H_4
	1255	4-$Me_2NCH_2C_6H_4$	3-HOC_6H_4
	1256	4-$Me_2NCH_2C_6H_4$	3,4-diHOC_6H_4
	1257	4-$Me_2NCH_2C_6H_4$	4-$NH_2CH_2C_6H_4$
	1258	4-$Me_2NCH_2C_6H_4$	3-$NH_2CH_2C_6H_4$
	1259	H	4-$MeOC_6H_4$
	1260	H	3-$MeOC_6H_4$
	1261	H	4-$NH_2C_6H_4$
	1262	H	3-$NH_2C_6H_4$
	1263	H	2-$NH_2C_6H_4$
	1264	H	4-$Me_2NC_6H_4$
	1265	H	3-$Me_2NC_6H_4$
	1266	H	2-$Me_2NC_6H_4$
	1267	H	4-pyridyl
	1268	H	3-pyridyl
	1269	H	2-pyridyl
	1270	H	2-thiazolyl
	1271	H	2-pyrazolyl
	1272	H	5-isoquinolyl
	1273	H	3,4-methylenedioxyC_6H_3
	1274	H	3,4-ethylenedioxyC_6H_3
	1275	H	2-imidazolyl
	1276	H	2-oxazolyl
	1277	H	4-isoxazolyl
	1278	H	4-HOC_6H_4
	1279	H	3-HOC_6H_4

1280	H	3,4-diHOC$_6$H$_4$
1281	H	4-NH$_2$CH$_2$C$_6$H$_4$
1282	H	3-NH$_2$CH$_2$C$_6$H$_4$
1283	Me	4-MeOC$_6$H$_4$
1284	Me	3-MeOC$_6$H$_4$
1285	Me	4-NH$_2$C$_6$H$_4$
1286	Me	3-NH$_2$C$_6$H$_4$
1287	Me	2-NH$_2$C$_6$H$_4$
1288	Me	4-Me$_2$NC$_6$H$_4$
1289	Me	3-Me$_2$NC$_6$H$_4$
1290	Me	2-Me$_2$NC$_6$H$_4$
1291	Me	4-pyridyl
1292	Me	3-pyridyl
1293	Me	2-pyridyl
1294	Me	2-thiazolyl
1295	Me	2-pyrazolyl
1296	Me	5-isoquinolyl
1297	Me	3,4-methylenedioxyC$_6$H$_3$
1298	Me	3,4-ethylenedioxyC$_6$H$_3$
1299	Me	2-imidazolyl
1300	Me	2-oxazolyl
1301	Me	4-isoxazolyl
1302	Me	4-HOC$_6$H$_4$
1303	Me	3-HOC$_6$H$_4$
1304	Me	3,4-diHOC$_6$H$_4$
1305	Me	4-NH$_2$CH$_2$C$_6$H$_4$
1306	Me	3-NH$_2$CH$_2$C$_6$H$_4$
1307	Et	4-MeOC$_6$H$_4$

1308	Et	3-$MeOC_6H_4$
1309	Et	4-$NH_2C_6H_4$
1310	Et	3-$NH_2C_6H_4$
1311	Et	2-$NH_2C_6H_4$
1312	Et	4-$Me_2NC_6H_4$
1313	Et	3-$Me_2NC_6H_4$
1314	Et	2-$Me_2NC_6H_4$
1315	Et	4-pyridyl
1316	Et	3-pyridyl
1317	Et	2-pyridyl
1318	Et	2-thiazolyl
1319	Et	2-pyrazolyl
1320	Et	5-isoquinolyl
1321	Et	3,4-methylenedioxyC_6H_3
1322	Et	3,4-ethylenedioxyC_6H_3
1323	Et	2-imidazolyl
1324	Et	2-oxazolyl
1325	Et	4-isoxazolyl
1326	Et	4-HOC_6H_4
1327	Et	3-HOC_6H_4
1328	Et	3,4-diHOC_6H_4
1329	Et	4-$NH_2CH_2C_6H_4$
1330	Et	3-$NH_2CH_2C_6H_4$
1331	2-$NH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1332	2-$NH_2C_6H_4CH_2$	3-$MeOC_6H_4$
1333	2-$NH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
1334	2-$NH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
1335	2-$NH_2C_6H_4CH_2$	2-$NH_2C_6H_4$

1336	2-$NH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
1337	2-$NH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
1338	2-$NH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
1339	2-$NH_2C_6H_4CH_2$	4-pyridyl
1340	2-$NH_2C_6H_4CH_2$	3-pyridyl
1341	2-$NH_2C_6H_4CH_2$	2-pyridyl
1342	2-$NH_2C_6H_4CH_2$	2-thiazolyl
1343	2-$NH_2C_6H_4CH_2$	2-pyrazolyl
1344	2-$NH_2C_6H_4CH_2$	5-isoquinolyl
1345	2-$NH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1346	2-$NH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1347	2-$NH_2C_6H_4CH_2$	2-imidazolyl
1348	2-$NH_2C_6H_4CH_2$	2-oxazolyl
1349	2-$NH_2C_6H_4CH_2$	4-isoxazolyl
1350	2-$NH_2C_6H_4CH_2$	4-HOC_6H_4
1351	2-$NH_2C_6H_4CH_2$	3-HOC_6H_4
1352	2-$NH_2C_6H_4CH_2$	3,4-diHOC_6H_4
1353	2-$NH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1354	2-$NH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1355	3-$NH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1356	3-$NH_2C_6H_4CH_2$	3-$MeOC_6H_4$
1357	3-$NH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
1358	3-$NH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
1359	3-$NH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
1360	3-$NH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
1361	3-$NH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
1362	3-$NH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$

	1363	3-$NH_2C_6H_4CH_2$	4-pyridyl
	1364	3-$NH_2C_6H_4CH_2$	3-pyridyl
	1365	3-$NH_2C_6H_4CH_2$	2-pyridyl
	1366	3-$NH_2C_6H_4CH_2$	2-thiazolyl
	1367	3-$NH_2C_6H_4CH_2$	2-pyrazolyl
	1367	3-$NH_2C_6H_4CH_2$	5-isoquinolyl
	1369	3-$NH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1370	3-$NH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1371	3-$NH_2C_6H_4CH_2$	2-imidazolyl
	1372	3-$NH_2C_6H_4CH_2$	2-oxazolyl
	1373	3-$NH_2C_6H_4CH_2$	4-isoxazolyl
	1374	3-$NH_2C_6H_4CH_2$	4-HOC_6H_4
	1375	3-$NH_2C_6H_4CH_2$	3-HOC_6H_4
	1376	3-$NH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	1377	3-$NH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1378	3-$NH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1379	4-$NH_2C_6H_4CH_2$	4-$MeOC_6H_4$
	1380	4-$NH_2C_6H_4CH_2$	3-$MeOC_6H_4$
	1381	4-$NH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
	1382	4-$NH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
	1383	4-$NH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
	1384	4-$NH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	1385	4-$NH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	1386	4-$NH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	1387	4-$NH_2C_6H_4CH_2$	4-pyridyl
	1388	4-$NH_2C_6H_4CH_2$	3-pyridyl
	1389	4-$NH_2C_6H_4CH_2$	2-pyridyl

	1390	4-$NH_2C_6H_4CH_2$	2-thiazolyl
	1391	4-$NH_2C_6H_4CH_2$	2-pyrazolyl
	1392	4-$NH_2C_6H_4CH_2$	5-isoquinolyl
	1393	4-$NH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1394	4-$NH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1395	4-$NH_2C_6H_4CH_2$	2-imidazolyl
	1396	4-$NH_2C_6H_4CH_2$	2-oxazolyl
	1397	4-$NH_2C_6H_4CH_2$	4-isoxazolyl
	1398	4-$NH_2C_6H_4CH_2$	4-HOC_6H_4
	1399	4-$NH_2C_6H_4CH_2$	3-HOC_6H_4
	1400	4-$NH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	1401	4-$NH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1402	4-$NH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1403	2-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$
	1404	2-$MeOC_6H_4CH_2$	3-$MeOC_6H_4$
	1405	2-$MeOC_6H_4CH_2$	4-$NH_2C_6H_4$
	1406	2-$MeOC_6H_4CH_2$	3-$NH_2C_6H_4$
	1407	2-$MeOC_6H_4CH_2$	2-$NH_2C_6H_4$
	1408	2-$MeOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	1409	2-$MeOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	1410	2-$MeOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	1411	2-$MeOC_6H_4CH_2$	4-pyridyl
	1412	2-$MeOC_6H_4CH_2$	3-pyridyl
	1413	2-$MeOC_6H_4CH_2$	2-pyridyl
	1414	2-$MeOC_6H_4CH_2$	2-thiazolyl
	1415	2-$MeOC_6H_4CH_2$	2-pyrazolyl
	1416	2-$MeOC_6H_4CH_2$	5-isoquinolyl

	1417	2-$MeOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1418	2-$MeOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1419	2-$MeOC_6H_4CH_2$	2-imidazolyl
	1420	2-$MeOC_6H_4CH_2$	2-oxazolyl
	1421	2-$MeOC_6H_4CH_2$	4-isoxazolyl
	1422	2-$MeOC_6H_4CH_2$	4-HOC_6H_4
	1423	2-$MeOC_6H_4CH_2$	3-HOC_6H_4
	1424	2-$MeOC_6H_4CH_2$	3,4-diHOC_6H_4
	1425	2-$MeOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1426	2-$MeOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1427	3-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$
	1428	3-$MeOC_6H_4CH_2$	3-$MeOC_6H_4$
	1429	3-$MeOC_6H_4CH_2$	4-$NH_2C_6H_4$
	1430	3-$MeOC_6H_4CH_2$	3-$NH_2C_6H_4$
	1431	3-$MeOC_6H_4CH_2$	2-$NH_2C_6H_4$
	1432	3-$MeOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	1433	3-$MeOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	1434	3-$MeOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	1435	3-$MeOC_6H_4CH_2$	4-pyridyl
	1436	3-$MeOC_6H_4CH_2$	3-pyridyl
	1437	3-$MeOC_6H_4CH_2$	2-pyridyl
	1438	3-$MeOC_6H_4CH_2$	2-thiazolyl
	1439	3-$MeOC_6H_4CH_2$	2-pyrazolyl
	1440	3-$MeOC_6H_4CH_2$	5-isoquinolyl
	1441	3-$MeOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3

1442	3-$MeOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1443	3-$MeOC_6H_4CH_2$	2-imidazolyl
1444	3-$MeOC_6H_4CH_2$	2-oxazolyl
1445	3-$MeOC_6H_4CH_2$	4-isoxazolyl
1446	3-$MeOC_6H_4CH_2$	4-HOC_6H_4
1447	3-$MeOC_6H_4CH_2$	3-HOC_6H_4
1448	3-$MeOC_6H_4CH_2$	3,4-diHOC_6H_4
1449	3-$MeOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1450	3-$MeOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1451	4-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$
1452	4-$MeOC_6H_4CH_2$	3-$MeOC_6H_4$
1453	4-$MeOC_6H_4CH_2$	4-$NH_2C_6H_4$
1454	4-$MeOC_6H_4CH_2$	3-$NH_2C_6H_4$
1455	4-$MeOC_6H_4CH_2$	2-$NH_2C_6H_4$
1456	4-$MeOC_6H_4CH_2$	4-$Me_2NC_6H_4$
1457	4-$MeOC_6H_4CH_2$	3-$Me_2NC_6H_4$
1458	4-$MeOC_6H_4CH_2$	2-$Me_2NC_6H_4$
1459	4-$MeOC_6H_4CH_2$	4-pyridyl
1460	4-$MeOC_6H_4CH_2$	3-pyridyl
1461	4-$MeOC_6H_4CH_2$	2-pyridyl
1462	4-$MeOC_6H_4CH_2$	2-thiazolyl
1463	4-$MeOC_6H_4CH_2$	2-pyrazolyl
1464	4-$MeOC_6H_4CH_2$	5-isoquinolyl
1465	4-$MeOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1466	4-$MeOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1467	4-$MeOC_6H_4CH_2$	2-imidazolyl

	1468	4-$MeOC_6H_4CH_2$	2-oxazolyl
	1469	4-$MeOC_6H_4CH_2$	4-isoxazolyl
	1470	4-$MeOC_6H_4CH_2$	4-HOC_6H_4
	1471	4-$MeOC_6H_4CH_2$	3-HOC_6H_4
	1472	4-$MeOC_6H_4CH_2$	3,4-diHOC_6H_4
	1473	4-$MeOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1474	4-$MeOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1475	2-$HOC_6H_4CH_2$	4-$MeOC_6H_4$
	1476	2-$HOC_6H_4CH_2$	3-$MeOC_6H_4$
	1477	2-$HOC_6H_4CH_2$	4-$NH_2C_6H_4$
	1478	2-$HOC_6H_4CH_2$	3-$NH_2C_6H_4$
	1479	2-$HOC_6H_4CH_2$	2-$NH_2C_6H_4$
	1480	2-$HOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	1481	2-$HOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	1482	2-$HOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	1483	2-$HOC_6H_4CH_2$	4-pyridyl
	1484	2-$HOC_6H_4CH_2$	3-pyridyl
	1485	2-$HOC_6H_4CH_2$	2-pyridyl
	1486	2-$HOC_6H_4CH_2$	2-thiazolyl
	1487	2-$HOC_6H_4CH_2$	2-pyrazolyl
	1488	2-$HOC_6H_4CH_2$	5-isoquinolyl
	1489	2-$HOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1490	2-$HOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1491	2-$HOC_6H_4CH_2$	2-imidazolyl
	1492	2-$HOC_6H_4CH_2$	2-oxazolyl
	1493	2-$HOC_6H_4CH_2$	4-isoxazolyl
	1494	2-$HOC_6H_4CH_2$	4-HOC_6H_4

1495	2-$HOC_6H_4CH_2$	3-HOC_6H_4
1496	2-$HOC_6H_4CH_2$	3,4-diHOC_6H_4
1497	2-$HOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1498	2-$HOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1499	3-$HOC_6H_4CH_2$	4-$MeOC_6H_4$
1500	3-$HOC_6H_4CH_2$	3-$MeOC_6H_4$
1501	3-$HOC_6H_4CH_2$	4-$NH_2C_6H_4$
1502	3-$HOC_6H_4CH_2$	3-$NH_2C_6H_4$
1503	3-$HOC_6H_4CH_2$	2-$NH_2C_6H_4$
1504	3-$HOC_6H_4CH_2$	4-$Me_2NC_6H_4$
1505	3-$HOC_6H_4CH_2$	3-$Me_2NC_6H_4$
1506	3-$HOC_6H_4CH_2$	2-$Me_2NC_6H_4$
1507	3-$HOC_6H_4CH_2$	4-pyridyl
1508	3-$HOC_6H_4CH_2$	3-pyridyl
1509	3-$HOC_6H_4CH_2$	2-pyridyl
1510	3-$HOC_6H_4CH_2$	2-thiazolyl
1511	3-$HOC_6H_4CH_2$	2-pyrazolyl
1512	3-$HOC_6H_4CH_2$	5-isoquinolyl
1513	3-$HOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1514	3-$HOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1514	3-$HOC_6H_4CH_2$	2-imidazolyl
1516	3-$HOC_6H_4CH_2$	2-oxazolyl
1517	3-$HOC_6H_4CH_2$	4-isoxazolyl
1518	3-$HOC_6H_4CH_2$	4-HOC_6H_4
1519	3-$HOC_6H_4CH_2$	3-HOC_6H_4
1520	3-$HOC_6H_4CH_2$	3,4-diHOC_6H_4
1521	3-$HOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$

	1522	3-$HOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1523	4-$HOC_6H_4CH_2$	4-$MeOC_6H_4$
	1524	4-$HOC_6H_4CH_2$	3-$MeOC_6H_4$
	1525	4-$HOC_6H_4CH_2$	4-$NH_2C_6H_4$
	1526	4-$HOC_6H_4CH_2$	3-$NH_2C_6H_4$
	1527	4-$HOC_6H_4CH_2$	2-$NH_2C_6H_4$
	1528	4-$HOC_6H_4CH_2$	4-$Me_2NC_6H_4$
	1529	4-$HOC_6H_4CH_2$	3-$Me_2NC_6H_4$
	1530	4-$HOC_6H_4CH_2$	2-$Me_2NC_6H_4$
	1531	4-$HOC_6H_4CH_2$	4-pyridyl
	1532	4-$HOC_6H_4CH_2$	3-pyridyl
	1533	4-$HOC_6H_4CH_2$	2-pyridyl
	1534	4-$HOC_6H_4CH_2$	2-thiazolyl
	1535	4-$HOC_6H_4CH_2$	2-pyrazolyl
	1536	4-$HOC_6H_4CH_2$	5-isoquinolyl
	1537	4-$HOC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1538	4-$HOC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1539	4-$HOC_6H_4CH_2$	2-imidazolyl
	1540	4-$HOC_6H_4CH_2$	2-oxazolyl
	1541	4-$HOC_6H_4CH_2$	4-isoxazolyl
	1542	4-$HOC_6H_4CH_2$	4-HOC_6H_4
	1543	4-$HOC_6H_4CH_2$	3-HOC_6H_4
	1544	4-$HOC_6H_4CH_2$	3,4-diHOC_6H_4
	1545	4-$HOC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1546	4-$HOC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1547	4-$ClC_6H_4CH_2$	4-$MeOC_6H_4$
	1548	4-$ClC_6H_4CH_2$	3-$MeOC_6H_4$

1549	4-$ClC_6H_4CH_2$	4-$NH_2C_6H_4$
1550	4-$ClC_6H_4CH_2$	3-$NH_2C_6H_4$
1551	4-$ClC_6H_4CH_2$	2-$NH_2C_6H_4$
1552	4-$ClC_6H_4CH_2$	4-$Me_2NC_6H_4$
1553	4-$ClC_6H_4CH_2$	3-$Me_2NC_6H_4$
1554	4-$ClC_6H_4CH_2$	2-$Me_2NC_6H_4$
1555	4-$ClC_6H_4CH_2$	4-pyridyl
1556	4-$ClC_6H_4CH_2$	3-pyridyl
1557	4-$ClC_6H_4CH_2$	2-pyridyl
1558	4-$ClC_6H_4CH_2$	2-thiazolyl
1559	4-$ClC_6H_4CH_2$	2-pyrazolyl
1560	4-$ClC_6H_4CH_2$	5-isoquinolyl
1561	4-$ClC_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1562	4-$ClC_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1563	4-$ClC_6H_4CH_2$	2-imidazolyl
1564	4-$ClC_6H_4CH_2$	2-oxazolyl
1565	4-$ClC_6H_4CH_2$	4-isoxazolyl
1566	4-$ClC_6H_4CH_2$	4-HOC_6H_4
1567	4-$ClC_6H_4CH_2$	3-HOC_6H_4
1568	4-$ClC_6H_4CH_2$	3,4-diHOC_6H_4
1569	4-$ClC_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1570	4-$ClC_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1571	2-$NH_2CH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1572	2-$NH_2CH_2C_6H_4CH_2$	3-$MeOC_6H_4$
1573	2-$NH_2CH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
1574	2-$NH_2CH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
1575	2-$NH_2CH_2C_6H_4CH_2$	2-$NH_2C_6H_4$

1576	2-$NH_2CH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
1577	2-$NH_2CH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
1578	2-$NH_2CH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
1579	2-$NH_2CH_2C_6H_4CH_2$	4-pyridyl
1580	2-$NH_2CH_2C_6H_4CH_2$	3-pyridyl
1581	2-$NH_2CH_2C_6H_4CH_2$	2-pyridyl
1582	2-$NH_2CH_2C_6H_4CH_2$	2-thiazolyl
1583	2-$NH_2CH_2C_6H_4CH_2$	2-pyrazolyl
1584	2-$NH_2CH_2C_6H_4CH_2$	5-isoquinolyl
1585	2-$NH_2CH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1586	2-$NH_2CH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1587	2-$NH_2CH_2C_6H_4CH_2$	2-imidazolyl
1588	2-$NH_2CH_2C_6H_4CH_2$	2-oxazolyl
1589	2-$NH_2CH_2C_6H_4CH_2$	4-isoxazolyl
1590	2-$NH_2CH_2C_6H_4CH_2$	4-HOC_6H_4
1591	2-$NH_2CH_2C_6H_4CH_2$	3-HOC_6H_4
1592	2-$NH_2CH_2C_6H_4CH_2$	3,4-diHOC_6H_4
1593	2-$NH_2CH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1594	2-$NH_2CH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1595	3-$NH_2CH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1596	3-$NH_2CH_2C_6H_4CH_2$	3-$MeOC_6H_4$
1597	3-$NH_2CH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
1598	3-$NH_2CH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
1599	3-$NH_2CH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
1600	3-$NH_2CH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
1601	3-$NH_2CH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
1602	3-$NH_2CH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$

	1603	3-$NH_2CH_2C_6H_4CH_2$	4-pyridyl
	1604	3-$NH_2CH_2C_6H_4CH_2$	3-pyridyl
	1605	3-$NH_2CH_2C_6H_4CH_2$	2-pyridyl
	1606	3-$NH_2CH_2C_6H_4CH_2$	2-thiazolyl
	1607	3-$NH_2CH_2C_6H_4CH_2$	2-pyrazolyl
	1608	3-$NH_2CH_2C_6H_4CH_2$	5-isoquinolyl
	1609	3-$NH_2CH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1610	3-$NH_2CH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1611	3-$NH_2CH_2C_6H_4CH_2$	2-imidazolyl
	1612	3-$NH_2CH_2C_6H_4CH_2$	2-oxazolyl
	1613	3-$NH_2CH_2C_6H_4CH_2$	4-isoxazolyl
	1614	3-$NH_2CH_2C_6H_4CH_2$	4-HOC_6H_4
	1615	3-$NH_2CH_2C_6H_4CH_2$	3-HOC_6H_4
	1616	3-$NH_2CH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	1617	3-$NH_2CH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1618	3-$NH_2CH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1619	4-$NH_2CH_2C_6H_4CH_2$	4-$MeOC_6H_4$
	1620	4-$NH_2CH_2C_6H_4CH_2$	3-$MeOC_6H_4$
	1621	4-$NH_2CH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
	1622	4-$NH_2CH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
	1623	4-$NH_2CH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
	1624	4-$NH_2CH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	1625	4-$NH_2CH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	1626	4-$NH_2CH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	1627	4-$NH_2CH_2C_6H_4CH_2$	4-pyridyl
	1628	4-$NH_2CH_2C_6H_4CH_2$	3-pyridyl
	1629	4-$NH_2CH_2C_6H_4CH_2$	2-pyridyl

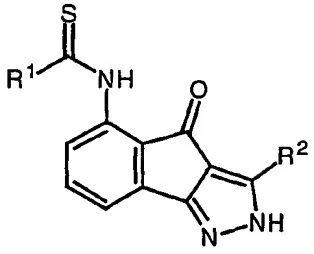
	1630	4-$NH_2CH_2C_6H_4CH_2$	2-thiazolyl
	1631	4-$NH_2CH_2C_6H_4CH_2$	2-pyrazolyl
	1632	4-$NH_2CH_2C_6H_4CH_2$	5-isoquinolyl
	1633	4-$NH_2CH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
	1634	4-$NH_2CH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
	1635	4-$NH_2CH_2C_6H_4CH_2$	2-imidazolyl
	1636	4-$NH_2CH_2C_6H_4CH_2$	2-oxazolyl
	1637	4-$NH_2CH_2C_6H_4CH_2$	4-isoxazolyl
	1638	4-$NH_2CH_2C_6H_4CH_2$	4-HOC_6H_4
	1639	4-$NH_2CH_2C_6H_4CH_2$	3-HOC_6H_4
	1640	4-$NH_2CH_2C_6H_4CH_2$	3,4-diHOC_6H_4
	1641	4-$NH_2CH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
	1642	4-$NH_2CH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
	1643	2-$Me_2NCH_2C_6H_4CH_2$	4-$MeOC_6H_4$
	1644	2-$Me_2NCH_2C_6H_4CH_2$	3-$MeOC_6H_4$
	1645	2-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
	1646	2-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
	1647	2-$Me_2NCH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
	1648	2-$Me_2NCH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
	1649	2-$Me_2NCH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
	1650	2-$Me_2NCH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
	1651	2-$Me_2NCH_2C_6H_4CH_2$	4-pyridyl
	1652	2-$Me_2NCH_2C_6H_4CH_2$	3-pyridyl
	1653	2-$Me_2NCH_2C_6H_4CH_2$	2-pyridyl
	1654	2-$Me_2NCH_2C_6H_4CH_2$	2-thiazolyl
	1655	2-$Me_2NCH_2C_6H_4CH_2$	2-pyrazolyl
	1656	2-$Me_2NCH_2C_6H_4CH_2$	5-isoquinolyl

1657	2-$Me_2NCH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1658	2-$Me_2NCH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1659	2-$Me_2NCH_2C_6H_4CH_2$	2-imidazolyl
1660	2-$Me_2NCH_2C_6H_4CH_2$	2-oxazolyl
1661	2-$Me_2NCH_2C_6H_4CH_2$	4-isoxazolyl
1662	2-$Me_2NCH_2C_6H_4CH_2$	4-HOC_6H_4
1663	2-$Me_2NCH_2C_6H_4CH_2$	3-HOC_6H_4
1664	2-$Me_2NCH_2C_6H_4CH_2$	3,4-diHOC_6H_4
1665	2-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1666	2-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1667	3-$Me_2NCH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1668	3-$Me_2NCH_2C_6H_4CH_2$	3-$MeOC_6H_4$
1669	3-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
1670	3-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
1671	3-$Me_2NCH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
1672	3-$Me_2NCH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
1673	3-$Me_2NCH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
1674	3-$Me_2NCH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
1675	3-$Me_2NCH_2C_6H_4CH_2$	4-pyridyl
1676	3-$Me_2NCH_2C_6H_4CH_2$	3-pyridyl
1677	3-$Me_2NCH_2C_6H_4CH_2$	2-pyridyl
1678	3-$Me_2NCH_2C_6H_4CH_2$	2-thiazolyl
1679	3-$Me_2NCH_2C_6H_4CH_2$	2-pyrazolyl
1680	3-$Me_2NCH_2C_6H_4CH_2$	5-isoquinolyl
1681	3-$Me_2NCH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3

1682	3-$Me_2NCH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1683	3-$Me_2NCH_2C_6H_4CH_2$	2-imidazolyl
1684	3-$Me_2NCH_2C_6H_4CH_2$	2-oxazolyl
1685	3-$Me_2NCH_2C_6H_4CH_2$	4-isoxazolyl
1686	3-$Me_2NCH_2C_6H_4CH_2$	4-HOC_6H_4
1687	3-$Me_2NCH_2C_6H_4CH_2$	3-HOC_6H_4
1688	3-$Me_2NCH_2C_6H_4CH_2$	3,4-diHOC_6H_4
1689	3-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1690	3-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$
1691	4-$Me_2NCH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1692	4-$Me_2NCH_2C_6H_4CH_2$	3-$MeOC_6H_4$
1693	4-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2C_6H_4$
1694	4-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2C_6H_4$
1695	4-$Me_2NCH_2C_6H_4CH_2$	2-$NH_2C_6H_4$
1696	4-$Me_2NCH_2C_6H_4CH_2$	4-$Me_2NC_6H_4$
1697	4-$Me_2NCH_2C_6H_4CH_2$	3-$Me_2NC_6H_4$
1698	4-$Me_2NCH_2C_6H_4CH_2$	2-$Me_2NC_6H_4$
1699	4-$Me_2NCH_2C_6H_4CH_2$	4-pyridyl
1700	4-$Me_2NCH_2C_6H_4CH_2$	3-pyridyl
1701	4-$Me_2NCH_2C_6H_4CH_2$	2-pyridyl
1702	4-$Me_2NCH_2C_6H_4CH_2$	2-thiazolyl
1703	4-$Me_2NCH_2C_6H_4CH_2$	2-pyrazolyl
1704	4-$Me_2NCH_2C_6H_4CH_2$	5-isoquinolyl
1705	4-$Me_2NCH_2C_6H_4CH_2$	3,4-methylenedioxyC_6H_3
1706	4-$Me_2NCH_2C_6H_4CH_2$	3,4-ethylenedioxyC_6H_3
1707	4-$Me_2NCH_2C_6H_4CH_2$	2-imidazolyl

1708		4-$Me_2NCH_2C_6H_4CH_2$	2-oxazolyl
1709		4-$Me_2NCH_2C_6H_4CH_2$	4-isoxazolyl
1710		4-$Me_2NCH_2C_6H_4CH_2$	4-HOC_6H_4
1711		4-$Me_2NCH_2C_6H_4CH_2$	3-HOC_6H_4
1712		4-$Me_2NCH_2C_6H_4CH_2$	3,4-diHOC_6H_4
1713		4-$Me_2NCH_2C_6H_4CH_2$	4-$NH_2CH_2C_6H_4$
1714		4-$Me_2NCH_2C_6H_4CH_2$	3-$NH_2CH_2C_6H_4$

Table 4



Example Number	R^1	R^2
1715	Methyl	4-$MeOC_6H_4$
1716	$ClCH_2$	4-$MeOC_6H_4$
1717	Cyclopropyl	4-$MeOC_6H_4$
1718	Isopropyl	4-$MeOC_6H_4$
1719	Ethyl	4-$MeOC_6H_4$
1720	Cyclopentyl	4-$MeOC_6H_4$
1721	Cyclobutyl	4-$MeOC_6H_4$
1722	Benzyl	4-$MeOC_6H_4$
1723	n-propyl	4-$MeOC_6H_4$
1724	4-$ClC_6H_4CH_2$	4-$MeOC_6H_4$
1725	3-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$
1726	4-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$

1727	3,4-diMeOC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1728	2,5-diMeOC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1729	Methyl	2-MeOC$_6$H$_4$
1730	Methyl	3,4-diMeOC$_6$H$_4$
1731	3,4-(OCH$_2$O)C$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1732	3-thiophenylCH$_2$	4-MeOC$_6$H$_4$
1733	2-MeOC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1734	3,4-diClOC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1735	2,4-diClOC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1736	2-ClC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1737	H$_2$NCH$_2$	4-MeOC$_6$H$_4$
1738	HOCH$_2$NHCH$_2$CH$_2$	4-MeOC$_6$H$_4$
1739	Me$_2$NCH$_2$	4-MeOC$_6$H$_4$
1740	PiperazinylCH$_2$	4-MeOC$_6$H$_4$
1741	4-Me-piperazinylCH$_2$	4-MeOC$_6$H$_4$
1742	4-HOCH$_2$CH$_2$-piperazinylCH$_2$	4-MeOC$_6$H$_4$
1743	PiperidinylCH$_2$	4-MeOC$_6$H$_4$
1744	4-NH$_2$CH$_2$-piperidinylCH$_2$	4-MeOC$_6$H$_4$
1745	CH$_3$CH$_2$NHCH$_2$	4-MeOC$_6$H$_4$
1746	ThiomorpholinylCH$_2$	4-MeOC$_6$H$_4$
1747	MorpholinylCH$_2$	4-MeOC$_6$H$_4$
1748	PyyrolidinylCH$_2$	4-MeOC$_6$H$_4$
1749	4-pyridylCH$_2$NHCH$_2$	4-MeOC$_6$H$_4$
1750	4-CH$_3$CONHC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1751	4-CH$_3$OCONHC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$
1752	4-NH$_2$CH$_2$CONHC$_6$H$_4$CH$_2$	4-MeOC$_6$H$_4$

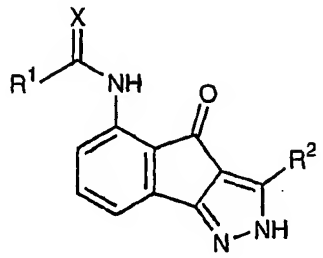
1753	4-$Me_2NCH_2CONHC_6H_4CH_2$	4-$MeOC_6H_4$
1754	4-$N_3C_6H_4CH_2$	4-$MeOC_6H_4$
1755	4-$NH_2C_6H_4CH_2$	4-$MeOC_6H_4$
1756	C_6H_5NH	4-$MeOC_6H_4$
1757	$CH_3CH_2CH_2NH$	4-$MeOC_6H_4$
1758	4-$NH_2C_6H_4CH_2NH$	4-$MeOC_6H_4$
1759	4-pyridyCH_2NH	4-$MeOC_6H_4$
1760	Methyl	4-HOC_6H_4
1761	H	4-$MeOC_6H_4$
1762	Methyl	3-pyridyl
1763	Methyl	4-pyridyl
1764	H	4-pyridyl
1765	Methyl	C_6H_5
1766	Methyl	4-$MeSC_6H_4$
1767	Methyl	4-$MeSO_2C_6H_4$
1768	Methyl	4-$Me_2NC_6H_4$
1769	MorpholinylCH_2	4-$Me_2NC_6H_4$
1770	Me_2NCH_2	4-$Me_2NC_6H_4$
1771	Me_2NCH_2	4-(piperdinyl)C_6H_4
1772	Me_2NCH_2	4-(morpholinyl)C_6H_4
1773	Me_2NCH_2	4-$CH_3CH_2OC_6H_4$
1774	Me_2NCH_2	4-$CH_3CH_2CH_2CH_2C_6H_4$
1775	Me_2NCH_2	4-$CH_3CH_2C_6H_4$
1776	Me_2NCH_2	4-$CH_3CH_2CH_2C_6H_4$

5

CLAIMS

What is claimed is:

1. A compound according to formula (I):



(I)

or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

X is selected from the group: O, S, and NR;

R is selected from the group: H, C_{1-4} alkyl, and NR^5R^{5a};

R^1 is selected from the group: H, C_{1-10} alkyl substituted with 0-3 R^c, C_{2-10} alkenyl substituted with 0-3 R^c, C_{2-10} alkynyl substituted with 0-3 R^c, C_{1-10} alkoxy, -NHR^4, C_{3-10} carbocycle substituted with 0-5 R^a, and 3-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^2 is selected from the group: H, C_{1-10} alkyl substituted with 0-3 R^c, C_{2-10} alkenyl substituted with 0-3 R^c,

C_{2-10} alkynyl substituted with 0-3 R^c, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^a, and 3-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, benzyl, C_{1-4} alkyl substituted with 1-3 R^c, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6; and

provided that if R^3 is phenyl, it is substituted with 1-5 R^a;

R^4 is independently at each occurrence selected from the group: H, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

provided that at least one R^3 is present and that this R^3 is selected from the group: C_{1-4} alkyl substituted with 1-3 R^6, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6;

R^a is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

alternatively, when two R^a's are present on adjacent carbon atoms they combine to form $-OCH_2O-$ or $-OCH_2CH_2O-$;

R^b is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, and SO_2R^{3b};

R^c is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^5NR^5R^{5a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

alternatively, R^3 and R^{3a}, together with the nitrogen atom to which they are attached, form a heterocycle having 4-8 atoms in the ring containing an additional 0-1 N, S, or O atom and substituted with 0-3 R^{3c};

R^{3b} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{3c} is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3b}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3b}$, $NHC(O)NR^3R^{3b}$, $NHC(S)NR^3R^{3b}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $SO_2NR^3R^{3b}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

R^5 is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5a} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5b} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^6 is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^5R^5, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{3-10} carbocycle substituted with 0-5 R^5, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^5; and

m is selected from 0, 1, 2, and 3.

2. A compound according to claim 1, wherein:

X is selected from the group: O, S, and NR;

R is selected from the group: H, C_{1-4} alkyl, and NR^5R^{5a};

R^1 is selected from the group: H, C_{1-5} alkyl substituted with 0-3 R^c, C_{2-5} alkenyl substituted with 0-3 R^c, C_{2-5}

alkynyl substituted with 0-3 R^c, $-NHR^4$, C_{3-6} carbocycle substituted with 0-5 R^a, and 3-6 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^2 is selected from the group: H, C_{1-5} alkyl substituted with 0-3 R^c, C_{2-5} alkenyl substituted with 0-3 R^c, C_{2-5} alkynyl substituted with 0-3 R^c, $-(CF_2)_mCF_3$, C_{3-6} carbocycle substituted with 0-5 R^a, and 3-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, benzyl, C_{1-4} alkyl substituted with 1-3 R^c, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6; and

provided that if R^3 is phenyl, it is substituted with 1-5 R^a;

R^4 is independently at each occurrence selected from the group: H, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

provided that at least one R^3 is present and that this R^3 is selected from the group: C_{1-4} alkyl substituted with 1-3 R^6, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6;

R^a is independently at each occurrence selected from the group: halo, -CN, N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

alternatively, when two R^a's are present on adjacent carbon atoms they combine to form $-OCH_2O-$ or $-OCH_2CH_2O-$;

R^b is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, and SO_2R^{3b};

R^c is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $NR^5NR^5R^{5a}$, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

alternatively, R^3 and R^{3a}, together with the nitrogen atom to which they are attached, form a heterocycle having 4-8 atoms in the ring containing an additional 0-1 N, S, or O atom and substituted with 0-3 R^{3c};

R^{3b} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{3c} is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4}

haloalkyl, NR^3R^{3b}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3b}$, $NHC(O)NR^3R^{3b}$, $NHC(S)NR^3R^{3b}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $SO_2NR^3R^{3b}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

R^5 is independently selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{5a} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5b} is independently selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^6 is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^5R^5, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{3-10} carbocycle substituted with 0-5 R^5, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^5; and

m is selected from 0, 1, 2, and 3.

3. A compound according to claim 2, wherein:

X is selected from the group: O and S;

R^1 is selected from the group: H, C_{1-5} alkyl substituted with 0-3 R^c, C_{2-5} alkenyl substituted with 0-3 R^c, $-NHR^4$, C_{3-6} carbocycle substituted with 0-5 R^a, and 3-6 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^2 is selected from the group: H, C_{1-5} alkyl substituted with 0-3 R^c, C_{2-5} alkenyl substituted with 0-3 R^c, $-(CF_2)_mCF_3$, C_{3-6} carbocycle substituted with 0-5 R^a, and 3-6 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, benzyl, C_{1-4} alkyl substituted with 1-3 R^c, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6; and

provided that if R^3 is phenyl, it is substituted with 1-5 R^a;

R^4 is independently at each occurrence selected from the group: H, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

provided that at least one R^3 is present and that this R^3 is selected from the group: C_{1-4} alkyl substituted with 1-3 R^6, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6;

R^a is independently at each occurrence selected from the group: halo, -CN, N_3, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

alternatively, when two R^a's are present on adjacent carbon atoms they combine to form -OCH_2O- or -OCH_2CH_2O-;

R^b is independently at each occurrence selected from the group: halo, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, and SO_2R^{3b};

R^c is independently at each occurrence selected from the group: halo, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^5NR^5R^{5a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

alternatively, R^3 and R^{3a}, together with the nitrogen atom to which they are attached, form a heterocycle having 5-6 atoms in the ring containing an additional 0-1 N, S, or O atom and substituted with 0-3 R^{3c};

R^{3b} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{3c} is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3b}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3b}$, $NHC(O)NR^3R^{3b}$, $NHC(S)NR^3R^{3b}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $SO_2NR^3R^{3b}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

R^5 is independently selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{5a} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5b} is independently selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^6 is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^5R^5, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{3-10} carbocycle substituted with 0-5 R^5, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^5; and

m is selected from 0, 1, 2, and 3.

4. A compound according to claim 3, wherein:

X is selected from the group: O and S;

R^1 is selected from the group: H, C_{1-5} alkyl substituted with 0-2 R^c, $-NHR^4$, C_{3-6} carbocycle substituted with 0-5 R^a, and 5-6 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-5 R^b;

R^2 is selected from the group: H, C_{1-5} alkyl substituted with 0-3 R^c, $-(CF_2)_mCF_3$, C_{3-6} carbocycle substituted with 0-5 R^a, and 5-6 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S and substituted with 0-3 R^b;

R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, benzyl, C_{1-4} alkyl substituted with 1-3 R^c, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4

heteroatoms selected from O, N, and S, substituted with 0-3 R^6; and

provided that if R^3 is phenyl, it is substituted with 1-5 R^a;

R^4 is independently at each occurrence selected from the group: H, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $NHC(S)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

provided that at least one R^3 is present and that this R^3 is selected from the group: C_{1-4} alkyl substituted with 1-3 R^6, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6;

R^a is independently at each occurrence selected from the group: halo, -CN, N_3, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, and 5-6

membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

alternatively, when two R^a's are present on adjacent carbon atoms they combine to form $-OCH_2O-$ or $-OCH_2CH_2O-$;

R^b is independently at each occurrence selected from the group: halo, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, and SO_2R^{3b};

R^c is independently at each occurrence selected from the group: halo, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^5NR^5R^{5a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, $NHC(O)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-6 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

alternatively, R^3 and R^{3a}, together with the nitrogen atom to which they are attached, form a heterocycle having 5-6 atoms in the ring containing an additional 0-1 N, S, or O atom and substituted with 0-3 R^{3c};

R^{3b} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{3c} is independently at each occurrence selected from the group: halo, -CN , N_3, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3b}, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3b}$, $NHC(O)NR^3R^{3b}$, $NHC(S)NR^3R^{3b}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, $SO_2NR^3R^{3b}$, SO_2R^{3b}, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S;

R^5 is independently selected from the group: H and C_{1-4} alkyl;

R^{5a} is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5b} is independently selected from the group: H and C_{1-4} alkyl;

R^6 is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^5R^5, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{3-10} carbocycle substituted with 0-5 R^5, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^5; and

m is selected from 0, 1, 2, and 3.

5. A compound according to claim 1, wherein the compound is selected from:

(a) 3-(4-methoxyphenyl)-5-(2-benzoylhydrazinecarboxamido)indeno [1,2-c]pyrazol-4-one;

(b) 3-(4-methoxyphenyl)-5-(2-isonicotinoylhydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(c) 3-(4-methoxyphenyl)-5-(2-nictinoylhydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(d) 3-(4-methoxyphenyl)-5-(2-(3,4-dihydroxybenzoyl)hydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(e) 3-(4-methoxyphenyl)-5-(2-(4-hydroxybenzoyl)hydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(f) 3-(4-methoxyphenyl)-5-(2-(3-aminobenzoyl)hydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(g) 3-(4-methoxyphenyl)-5-(2-(4-aminobenzoyl)hydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(h) 3-(4-methoxyphenyl)-5-(2-(2-aminobenzoyl)hydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(i) 3-(4-methoxyphenyl)-5-(2-(4-N,N-dimethylaminobenzoyl) hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

(j) 3-(4-methoxyphenyl)-5-(2-phenethylacetylhydrazine carboxamido)indeno[1,2-c]pyrazol-4-one;

(k) 3-(4-methoxyphenyl)-5-(2-(2-hydroxybenzoyl)hydrazine carboxamido)indeno[1,2-c]pyrazol-4-one; and

(l) 3-(4-methoxyphenyl)-5-(2-methoxycarbonyl hydrazinecarboxamido)indeno[1,2-c]pyrazol-4-one;

(m) 1-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-3-morpholin-4-yl-urea;

(n) [3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-urea;

(o) 1-(2-amino-cyclohexyl)-3-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-urea;

(p) 2-(4-aminomethyl-piperidin-1-yl)-N-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-acetamide;

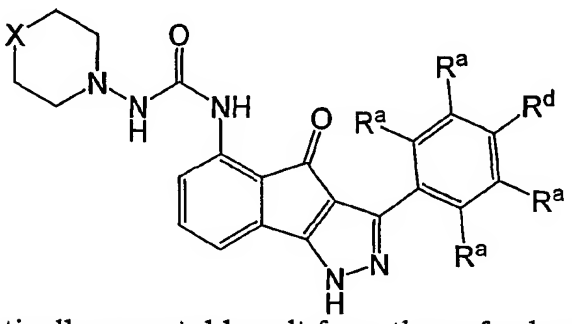
(q) 1-[3-(4-methoxy-phenyl)-4-oxo-2,4-dihydro-indeno[1,2-c]pyrazol-5-yl]-3-morpholin-4-yl-urea.

or a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1.

7. A method of treating cancer and proliferative diseases comprising: administering to a host in need of such treatment a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or prodrug form thereof.

8. A compound according to formula (II) :



or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

X is selected from the group: 0 and NR;

R is selected from the group: H, C_{1-4} alkyl, NR^3R^{3a}, and C_{1-4} alkyl substituted with 1-3 R^c;

R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, NHC (O) NR^5R^{5a}, NHC (S) NR^5R^{5a}, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, benzyl, C_{1-4} alkyl substituted with 1-3 R^c, C_{5-10} alkyl substituted with C_{2-10} alkenyl optionally substituted with 0-3 R^6, C_{2-10} alkynyl substituted with 0-3 R^6, $-(CF_2)_mCF_3$, C_{3-10} carbocycle substituted with 0-5 R^6, and 5-10

membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^6; and

provided that if R^3 is phenyl, it is substituted with 1-5 R^a;

R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{3b} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^5 is independently selected from the group: H, C_{1-4} alkyl, phenyl and benzyl;

R^{5a} is independently selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^{5b} is independently selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;

R^6 is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^5R^5, $NR^5NR^5R^{5a}$, $NR^5C(O)OR$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{3-10} carbocycle substituted with 0-5 R^5, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^5;

R^a is independently at each occurrence selected from the group: H, halo, C_{1-4} alkyl, NR^3R^{3a}, and R^3;

R^c is independently at each occurrence selected from the group: halo, -CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, NR^3R^{3a}, $NR^5NR^5R^{5a}$, $NR^3C(O)OR^3$, $NR^3C(O)R^3$, =O, OR^3, COR^3, CO_2R^3, $CONR^3R^{3a}$, NHC

(O) NR^3R^{3a}, NHC (S) NR^3R^{3a}, $SO_2NR^3R^{3a}$, SO_2R^{3b}, C_{3-10} carbocycle substituted with 0-5 R^a, and 5-10 membered heterocycle containing from 1-4 heteroatoms selected from O, N, and S, substituted with 0-3 R^3;

R^d is independently at each occurrence selected from the group: OR^3, COR^3, and NR^3R^{3a}; and

m is selected from 0, 1, 2, and 3.

9. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 8.

10. A method of treating cancer and proliferative diseases comprising: administering to a host in need of such treatment a therapeutically effective amount of a compound of claim 8, or a pharmaceutically acceptable salt or prodrug form thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/22663

BOX I. OBSERVATIONS WHERE CLAIMS WERE FOUND UNSEARCHABLE

2. Where no meaningful search could be carried out, specifically:

In these claims, the numerous variables (e.g. R1, R2, X, Rc, R4, Ra, Rb,R3, etc.) and their voluminous, complex meanings and their seemingly endless permutations and combinations plus the involved proviso sections and the lengthy list of named compounds (claim 6), make it virtually impossible to determine the full scope and complete meaning of the claimed subject matter. As presented, the claimed subject matter cannot be regarded as being a clear and concise description for which protection is sought and as such the listed claims do not comply with the requirements of PCT Article 6. Thus it is impossible to carry out a meaningful search on same. A search will be made on the first discernable invention of claim 5, the first compound therein.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/22663

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-4 and 6-10
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Please See Extra Sheet.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/22663

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07D 231/54

US CL :548/359.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 548/359.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	Database CAS ONLINE on STN, Chem. Abstr., Accession no. 2001: 6874444, Vol. 135, No. 242226, NUGIEL, D. et al, ' Preparation of a new acylsemicarbizide-containing indeno(1,2-c)pyrazol-4-ones as cyclin dependent kinase (cdk) inhibitors ', US 6291504, (2001/09/18), abstract.	5

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
05 MARCH 2003	07 APR 2003
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer R. W. RAMSUER
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet) (July 1998)*

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 January 2003 (30.01.2003)

PCT

(10) International Publication Number
WO 03/007883 A3

(51) International Patent Classification[7]: C07D 231/54

(21) International Application Number: PCT/US02/22663

(22) International Filing Date: 16 July 2002 (16.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/906,963 16 July 2001 (16.07.2001) US

(71) Applicant *(for all designated States except US)*: **BRISTOL-MYERS SQUIBB PHARMA COMPANY** [US/US]; P. O. Box 4000, Route 206 and Provinceline Road, Princeton, NJ 08543-4000 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **NUGIEL, David** [US/US]; 8 Vanessan Court, Cherry Hill, NJ 08003 (US). **CARINI, David** [US/US]; 1921 Julian Road, Wilmington, DE 19803 (US). **DIMEO, Susan** [US/US]; 406 Clayton Avenue, Wilmington, DE 19809 (US). **VIDWANS, Anup** [IN/US]; 25 Angelica Drive, Avondale, PA 19311 (US). **YUE, Eddy** [US/US]; 9 Altemus Drive, Landenberg, PA 19350 (US).

(74) Agents: **PATEL, Rena** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543-4000 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

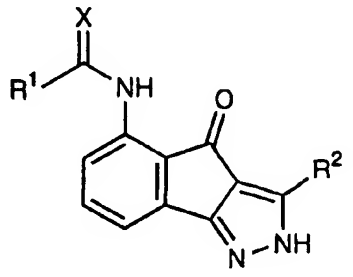
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
22 May 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ACYLSEMICARBAZIDES AS CYCLIN DEPENDENT KINASE INHIBITORS USEFUL AS ANTI-CANCER AND ANTI-PROLIFERATIVE AGENTS



(I)

(57) Abstract: The present invention relates to the synthesis of a new class of indeno[1,2-c]pyrazol-4-ones of formula (I) that are potent inhibitors of the class of enzymes known as cyclin dependent kinases, which relate to the catalytic subunits cdk1-7 and their regulatory subunits know as cyclins A-G. This invention also provides a novel method of treating cancer or other proliferative diseases by administering a therapeutically effective amount of one of these compounds or a pharmaceutically acceptable salt form thereof. Alternatively, one can treat cancer or other proliferative diseases by administering a therapeutically effective combination of one of the compounds of the present invention and one or more other known anti-cancer or anti-proliferative agents.

WO 03/007883 A3